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THE

MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—10TH YEAR. SYDNEY: SATURDAY, SEPTEMBER 22, 1923. No. 12.

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Table of Contents

ORIGINAL ARTICLES— PAGE.
"The Treatment of Typhoid Fever by Intravenous Vaccines," by K. DOUGLAS FAIRLEY, M.D. .. 291
REPORTS OF CASES—
"Primary Blasto-Mycotic Meningitis Occurring in a Child," by D. L. BARLOW, M.D., B.S. 302
REVIEWS—
Clinical Laboratory Methods 304
DEATH OF SIR WALTER DAVIDSON 305
LEADING ARTICLES—
The Depopulation of the Pacific 305
CURRENT COMMENT—
Intra-Cranial Aneurysms 306
Metastatic Tumours of Bone 307
ABSTRACTS FROM CURRENT MEDICAL LITERATURE—
Therapeutics 308
Urology 309
PAGE.
BRITISH MEDICAL ASSOCIATION NEWS—
Scientific 310
Nominations and Elections 316
CORRESPONDENCE—
"Insulin" 316
Removal of Tonsils 317
CONGRESS NOTES—
The Australasian Medical Congress (British Medical Association 318
MEDICAL MATTERS IN PARLIAMENT 318
MEDICAL APPOINTMENTS 318
MEDICAL APPOINTMENTS VACANT, ETC. 318
MEDICAL APPOINTMENTS: IMPORTANT NOTICE 318
DIARY FOR THE MONTH 318
EDITORIAL NOTICES 318

THE TREATMENT OF TYPHOID FEVER BY INTRAVENOUS VACCINES.

BY K. DOUGLAS FAIRLEY, M.D.,
From the Walter and Eliza Hall Institute of Research, Melbourne.

SOME ten years ago Thiroloix and Bardon[1] and Ichikawa[2] published results of the beneficial effects of the intravenous injection of a vaccine of *Bacillus typhosus* in the treatment of typhoid fever. Many observers in different countries have since confirmed their results. In Australia, however, this method of treatment has been but rarely adopted.

This paper is based on the results obtained with intravenous vaccine therapy in twenty-nine patients for whose treatment I was more or less directly responsible. The majority of these adults were in the wards of the Melbourne Hospital between February, 1921, and December, 1922. In addition the medical staffs of the Alfred and Children's Hospitals have allowed me to include the results of the treatment in twenty-four patients at these institutions in the past two years. These form an independent series for which I am in no way responsible. The larger number of cases recorded enables conclusions of greater value to be drawn and emphasizes the fact that more than one observer has obtained good results with this method of treatment of typhoid fever.

The control series comprise twenty-nine patients treated in the Melbourne and thirty treated in the Children's Hospital over the same period. The former comprises in the main a mild type of the disease, the three deaths in this series having occurred early in 1921 before the value of intravenous therapy was realized. After this all patients with serious infection were given the benefit of this form of treatment.

Table I. shows the results of the treatment in forty adults (over fifteen years of age) and in fifteen children (under fifteen years old) compared with the control series.

It is seen that in the adults the average febrile period was shortened by about ten days. The figures are too small to draw any definite conclusions from the mortality rates. The day on which the patient went to bed, was reckoned as the first day of the illness, unless a strong agglutination reaction in the serum indicated that the disease was of longer standing than such a calculation suggested. The insidious onset renders the accurate estimation of the duration of the disease very difficult.

In every patient but one the clinical diagnosis was confirmed by laboratory methods including the

TABLE I.—A COMPARISON OF TREATED AND UNTREATED CASES.

Series.	Number of Cases.	Age in Years.	Day of Disease on Admission.	Febrile Period After Admission in Days.	Total Febrile Period in Days.	Relapses.	Mortality Rate.
ADULTS—							
Own Series	29	26	11.5	14.4	25.9	3.4%	6.9%
Alfred Hospital	11	29.5	7.6	21.0	28.6	—	9.1%
Total	40	27	10.4	16.2	26.6	2.5%	7.5%
Control	29	31.5	12.9	23.6	36.5	3.4%	10.3%
CHILDREN—							
Children's Hospital	7	8.4	4.7	33.0	37.7	—	14.3%
Alfred Hospital	6	12	8.0	24.2	32.2	33.3%	16.7%
Others	2	14	10.0	17.5	27.5	—	—
Total	15	10.6	6.7	27.3	34.0	13.3%	13.3%
Control (Children's Hospital)	30	9.2	9.4	20.7	30.1	16.7%	6.7%

Widal reaction or the isolation of *Bacillus typhosus* from the patient or both.

The history and clinical picture of the one exception (Case No. 3) left no reasonable doubt that the condition belonged to the enteric group. This man was cured on the sixth day of the disease, while several of his relatives were still in hospital with typhoid fever.

Table II. gives a detailed analysis of the uncomplicated adult cases of the treated series. Cases 1 to 20 were, with three exceptions, under personal supervision, while Cases 30 to 40 were treated at the Alfred Hospital.

The former series shows that 75% of these patients were cured by crisis within five days of the first injection. Of those so cured who received more than one injection of the vaccine, the average interval between the injections was 1.8 days. Of the 25% whose pyrexia was less definitely influenced, the average interval between injections was three days. In the Alfred Hospital series the results are less striking, only two of eleven patients being cured by crisis. The average interval between injections in the remaining patients is four days.

It seems essential to give the vaccine daily or at least every alternate day if the best results are to be obtained.

There was one death, possibly due toxæmia, in the latter series (Case No. 40). No reaction followed the second vaccine given when the patient was practically moribund. As necropsy was not permitted and as there had been a complaint of abdominal pain two days before death, it is impossible to exclude the presence of some complication.

In the absence of complications the abolition or definite diminution of the toxæmic features of the disease following intravenous vaccine therapy is quite as remarkable as the effect on the pyrexia. Within four days even in those in whom the febrile course of the disease persists unchanged, the dull lethargic patient with anorexia, dry furred tongue and distended abdomen becomes mentally alert with a moist clean tongue, good appetite and abdomen of normal appearance.

Various effects of intravenous vaccine therapy on the temperature are shown in the accompanying charts (see page 294). In all cases after the final reading shown on the chart the temperature continued below normal for the remainder of the time the patient was in hospital.

The chart of Case No. 31 (Alfred Hospital series) shows the dramatic termination of the disease by crisis following a single injection of the vaccine on the ninth day of the illness. It also illustrates the fact that occasionally very low temperatures are recorded following these injections. In one case after two injections on successive days the temperature fell by crisis and for fourteen hours could not be recorded on a thermometer which did not register lower than 35° C. (95° F). The temperature thereafter remained below normal and the patient made an uninterrupted recovery.

The chart of Case No. XI. (Dr. Embleton's case) is recorded to show the hyperpyrexia which may occur following these injections. In this patient the result was excellent, the disease terminating by crisis on the ninth day of the illness.

Usually, however, these excessive reactions with very high or very low temperatures indicate that the febrile course of the disease will persist more or less unchanged, though the toxæmia may be diminished or abolished.

The chart of Case No. 30 (Alfred Hospital series) shows a cure by crisis on the ninth day of the disease, the reaction being of a mild intermediate type. These illustrations are purposely taken from cases not under personal observation to show that various observers have obtained these excellent results.

The chart of Case No. 15 shows a satisfactory response only after several injections of vaccine. The history is as follows.

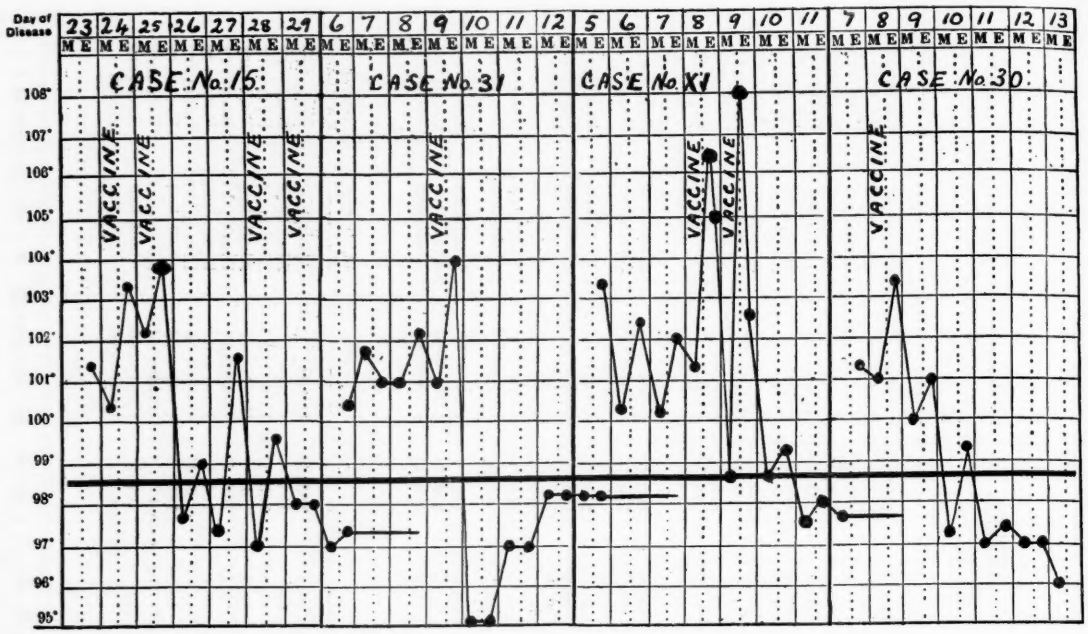
TABLE II.—THE UNCOMPLICATED ADULT CASES OF THE TREATED SERIES (OVER FIFTEEN YEARS OLD).

Case Number.	Days of Injection of Vaccine.	Days Febrile After First Vaccine.	Total Febrile Period.	Dosage of *Bacillus typhosus* (in Millions).	Type of Vaccine.	Maximum Temperature Attained in Any Reaction. C.	F.	Fever.	Toxæmia.	Result.
1	9	0	9	200	T.A.B.	40.5°	105°	Crisis	Abolished	Recovery
2	12	0	12	250	B.ty.	40.5°	105°	Crisis	Abolished	Recovery
3	4-5	1	5	175-250	T.A.B.	40.9°	105.6°	Crisis	Abolished	Recovery
4	10-11	1	11	75-150	B.ty.	41.1°	106.0°	Crisis	Abolished	Recovery
5	12	1	13	175	T.A.B.	39.8°	103.6°	Crisis	Abolished	Recovery
6	16	1	17	150	B.ty.	40.2°	104.4°	Crisis	Abolished	Recovery
7*	16	1	17	150	B.ty.	40.2°	104.4°	Crisis	Abolished	Recovery
8	34	1	35	90	B.ty.	39.6°	103.2°	Crisis	Abolished	Recovery
9	42	1	43	120	B.ty.	40.1°	104.2°	Crisis	Abolished	Recovery
10	8-9	2	10	200-250	B.ty.	41.2°	106.0°	Crisis	Abolished	Recovery
11*	8-9	2	10	150-175	B.ty.	42.2°	108.0°	Crisis	Abolished	Recovery
12	11-12-14-15	4	15 } 21	75-250	T.A.B.	40.8°	105.4°	Crisis	Abolished	Relapse
	Relapse 6	0	6 }	250	T.A.B.	40.5°	105°	Crisis	Abolished	Recovery
13	7-8-11	5	12	100-175	T.A.B.	40.5°	105°	Crisis	Abolished	Recovery
14	14-19-22	5	19	175	T.A.B.	40.8°	105.4°	Crisis	Abolished	Recovery
15	24-25-28-29	5	29	100-175	B.ty.	39.8°	103.6°	Crisis	Abolished	Recovery
				120	T.A.B.					
16*	8-12	8	16	50	B.ty.	40.5°	105°	Lysis	Abolished	Recovery
17	11-12-13-16-19-22	12	23	150-250	B.ty.	40.8°	105.4°	Decreased	Abolished	Recovery
				200	T.A.B.					
18	14-18-21	24	38	100-250	T.A.B.	40.5°	105°	Unaltered	Abolished	Recovery
19	10-12-16-20-22	26	36	75-200	T.A.B.	41.6°	106.8°	Unaltered	Abolished	Recovery
20	11-13-17-23-25	28	39	250	T.A.B.	41.3°	106.2°	Unaltered	Abolished	Carrier
Average		6.1	20.7	50-250						
30	8	1	9	100	T.A.B.	39.7°	103.4°	Crisis	Abolished	Recovery
31	9	1	10	160	T.A.B.	40°	104°	Crisis	Abolished	Recovery
32	8-11	13	21	150	T.A.B.	40.8°	105.4°	Lowered	Abolished	Recovery
33	5-9-13	17	22	150	T.A.B.	41.2°	106°	Unaltered	Abolished	Recovery
34	11-14-17	18	29	100-300	T.A.B.	41.4°	106.4°	Lowered	Diminished	Recovery
35	30-32-34-40-48	19	49	100-250	T.A.B.	40.2°	104.4°	Lowered	Diminished	Recovery
36	5-8-12-19	20	25	150	T.A.B.	42.4°	108.4°	Unaltered	Diminished	Recovery
37	14-20-23-29	25	39	100-180	T.A.B.	40.5°	105°	Unaltered	Abolished	Recovery
38	15	25	40	200	T.A.B.	No record.		Unaltered	No record	Recovery
39	6-10-13-15-17-21	36	42	100-160	T.A.B.	42°	107.6°	Unaltered	Abolished	Recovery
40	11-15	5	16	150-200	T.A.B.	No record.		Unaltered	Unaltered	Death
		17.5	28.6	100-300	T.A.B.					

B.ty. = Vaccine of *Bacillus typhosus*. T.A.B. = Vaccine of *Bacillus typhosus*, *Bacillus paratyphosus A* and *Bacillus paratyphosus B* in the proportions 2 : 1 : 1.

Note especially the column: "Days febrile after first vaccine."

*I am indebted to Dr. D. M. Embleton for the notes of Case No. 11 and to Mr. R. Hylton for those of Cases Nos. 7 and 16.



The patient was admitted in too toxic a state to give any account of his illness. *Bacillus typhosus* was isolated from the blood. The Widal reaction was obtained in a dilution of 1 in 640 with *Bacillus typhosus*.

The tongue was dry and furred, sordes being present on the lips and teeth. The pulse was rapid (one hundred per minute) and of low tension. The heart was enlarged, the apex beat being in the sixth interspace ten centimetres from the mid-line, while the right edge of the cardiac dulness extended 2.5 centimetres to the right of the right border of the sternum. The spleen was palpable and many typical rose spots were seen. The following night the patient was delirious and was constantly picking at the bed clothes. On each of the next two days an injection of one hundred million *Bacillus typhosus* vaccine was given intravenously. The temperature fell and the mental condition of the patient was greatly improved though the tongue remained dry.

Two nights later the temperature rose and the patient was delirious and violent all night, despite the injection of 0.02 gramme (a third of a grain) of morphine. Next day a dose of one hundred and twenty million *Bacillus typhosus* with sixty million each of *Bacilli paratyphosi A et B* was given intravenously with good effect and on the following day though the temperature was normal and the general condition of the patient was excellent a similar injection was given. From this time convalescence was uninterrupted.

In this severe case of typhoid fever with definite toxæmia temporary improvement, occurring after two vaccines had been given, became permanent after two more injections.

Table III. shows the results of this form of treatment in children from five to fifteen years old.

Excepting in the two patients who died, all these cases were apparently uncomplicated.

At the Alfred Hospital (where the average age of the patients was somewhat higher) large doses of the vaccine (average one hundred million) were given. At the Children's Hospital small doses (average twelve million) were used. In the few cases available for comparison there is little difference in the results of the two methods; hyperpyrexial reactions (over 40.8° C. or 105.5° F.) are equally frequent and the end results are much the same. In both cases the results are inferior to those obtained in older patients. Again the interval between injections is rather long, 3.7 days in the Children's Hospital cases (excluding Case No. 47) and 4.0 days in the Alfred Hospital series.

It would seem that particularly in the younger children considerable care is advisable with regard to dosage, while the vaccines should be given daily or at least every alternate day.

An attempt should also be made to avoid hyperpyrexial reactions by the means suggested later.

The Incidence of Complications in the Adults of the Two Series.

Tables IV. and V. show the incidence of complications in the adult patients (*id est* over fifteen years of age) of the treated and untreated series.

From Table IV. it is seen that three of the nine treated patients who developed complications, were afebrile in less than five days from the first injection of the vaccine only to become febrile again with the onset of some secondary or associated infection.

Hæmorrhage was less severe and not more frequent in the treated series. Formerly it was stated that vaccine therapy increased the risk of hæmorrhage, but this idea is steadily losing ground. Indeed, the rarity of any focal reaction following the intravenous injection of vaccine in these cases suggests that such a reaction, when it does occur, is accidental and quite independent of vaccine treatment.

The leucopenia, so characteristic of typhoid fever, is probably responsible for the high incidence of

TABLE III.—THE RESULTS OF INTRAVENOUS THERAPY IN FIFTEEN CHILDREN (UNDER FIFTEEN YEARS OF AGE).

TABLE III.—THE RESULTS OF INTRAVENOUS THERAPY IN FIFTEEN CHILDREN (UNDER FIFTEEN YEARS OF AGE).

Number of Case.	Age in Years.	Days of Injection of Vaccine.	Days Febrile After First Vaccine.	Total Febrile Period (Days).	Dosage in Millions of B.ty.	Type of Vaccine.	Maximum Temperature Reaction. C.	Maximum Temperature Reaction. F.	Fever.	Toxæmia.	Result.
41	12	13-18	6	19 } 43	50-100	T.A.B.	40.8°	105.4°	Crisis	Abolished	Relapse
		Relapse 5-10	19	24 }	200		40.3°	104.6°	Unaltered	Abolished	Recovery
42	12	4	11	15 } 24	10	T.A.B.	—	—	Lowered	Diminished	Relapse
		Relapse 8	1	9 }	50		40.9°	105.6°	Crisis	Abolished	Recovery
43	14	10	10	20	100	T.A.B.	40.5°	105°	Lowered	Abolished	Recovery
44	12	10-13-18	22	32	100-120	T.A.B.	41.4°	106.4°	Unaltered	Abolished	Recovery
45	14	9-11-15-18-21	33	42	100	T.A.B.	41.5°	106.6°	Unaltered	Diminished	Recovery
46	7	10-12-19	17	27	25-120	T.A.B.	—	—	Unaltered	Unaltered	Death Parotitis Cancrum Oris Pneumonia
Average ..	12	(1) Taking relapses as separate infections ..	14.6		10-200 Average 100						
		(2) Including relapses ..	23.0	32.2							
47[1]	6	23-24-25-26-29-30-31	8	31	5-10	B.ty.	41.2°	106°	Crisis after last injection	Diminished gradually	Recovery
48	10	9-10-17-18	18	27	10	B.ty.	40.9°	105.6°	Lowered	Abolished	Recovery
49	5	9	21	30	10	T.A.B.	39.5°	103.2°	Lowered	Unaltered Convulsion	Recovery
50	10	7-8-15	27	34	10	B.ty.	41.6°	106.8°	Unaltered	Diminished	Recovery
51	7	15	31	46	15	T.A.B.	40.9°	105.6°	Lowered	Diminished	Recovery
52	9	11-16	47	58	25	T.A.B.	40.8°	105.4°	Unaltered	Diminished	Recovery
53[1]	12	12	4	16	25	T.A.B.	41.7°	107°	Lowered	Increased	Death Pneumonia
Average ..	8.4		25.3	37.7	5-25 Average 12						
54[2]	14	12	1	13	75	B.ty.	—	—	Crisis	Abolished	Recovery
55[2]	14	16-19-23	26	42	50-75	B.ty.	41°	105.8°	Unaltered	Abolished	Recovery
Total ..	10.5										
Average ..		(a) Relapses separate ..	18.7	34.0							
		(b) Including relapses ..	22.6								

[1] In arriving at the average febrile periods (days), Cases Nos. 46 and 53 (where death resulted) are excluded; otherwise misleading results are obtained.
[2] I am indebted to Mr. R. Hylton for the notes of Cases Nos. 54 and 55.
The patients 41—46 were treated at the Alfred Hospital and the patients 47—53 were treated at the Children's Hospital.

TABLE IV.—THE COMPLICATIONS IN THE TREATED SERIES (ADULTS).

Case Number.	Days of Injection of Vaccine.	Days Febrile After First Vaccine.	Total Febrile Period (Days).	Dosage in Millions, (*Bacillus typhosus*).	Vaccine Used.	Maximum Temperature Reaction. C.	F.	Complications.	Result.
21	25-27-29	6	31	180-240	T.A.B.	40.5°	105°	Slight hæmorrhage, perforation	Death
22	30-31-33-34	5	35	50-80	B.ty.	40.5°	105°	Pneumonia	Death
23	8-9 14-16	1 28	9 37	200 200	T.A.B. T.A.B.	40.5° 40.5°	105° 105°	Slight hæmorrhage, cellulitis of face, orbit and scalp (*Staphylococcus aureus*)	Recovery with blindness of right eye
24	11-13-15-20-29	32	43	200-300	T.A.B.	41.1°	105.8°	Pyelitis (*Bacillus coli*)	Recovery
25	9-10-12-13-16	74	83	120-180 200-300	T.A.B. B.ty.	41.8° 40.5°	107.2° 105°	Thrombosis of the right femoral vein Pulmonary embolism, renal infarction	Recovery
26	10-11-12	3 4	13 17	120	B.ty.	41.8°	107.2°	Prostatic abscess (*Staphylococcus aureus*)	Recovery
27	15-16-17-23-26-30-32-34	2 18	17 35	120	B.ty.	41.2°	106°		Recovery
28	10-11-12-13-15-17-18	20	30	75-250	B.ty.	40.5°	105°	Slight hæmorrhage	Recovery
29	15-17-18-19-20-22-28	24	39	150-275	B.ty.	42°	107.6°	Hæmorrhage on admission	Recovery

In patient No. 25 acute gangrenous appendicitis developed during convalescence.
Case No. 27 was complicated by gonorrhœa with pelvic inflammation.
Where two series of figures appear in Cases 23, 26 and 27 in the Column "Days Febrile After First Vaccine," it indicates that before the rise of temperature due to the complication or the associated disease the patients had been afebrile for some days and apparently cured of the enteric infection.

secondary infections in the course of this disease. In both treated and untreated cases secondary infections were the cause of the majority of the complications. Vaccine therapy directed against *Bacillus typhosus* apparently does not lessen the incidence of these infections.

The toxæmia which accounted for the three deaths in the untreated series, was conspicuous by its absence in all treated patients except those with virulent secondary infections or other associated diseases.

Three adult patients succumbed despite intravenous vaccine therapy. One of these (Alfred Hospital series, No. 40) has already been considered. Of the two patients under personal supervision one (No. 21, an ambulatory patient) was admitted to hospital late in the fourth week of the disease. Two injections of vaccine at two day intervals caused a slight diminution of the toxæmia, but twenty hours after the third injection of the vaccine perforation of the ileum occurred. Four hours later the patient underwent operation, but on the following day he died. No treatment instituted after necrosis of the lymphoid tissue of the bowel has taken place, will prevent the separation of the slough and if the necrosis has extended to the peritoneum, perforation of the ulcer must follow when the slough separates. In this particular instance of an ambulatory patient coming under observation late in the fourth week of the disease, it was highly probable that perforation would occur. Though the dosage of the vaccine might without disadvantage have been smaller, vaccine therapy merely failed where any form of treatment would have been equally unsuccessful.

Early vaccine treatment will frequently abort the disease and thus prevent extension of the necrosis with the result that the slough involves only the superficial coats of the intestine. In this way alone can vaccine treatment lessen the liability to perforation of the bowel in this disease.

In the case of the other patient (No. 22) it was only when a fatal

TABLE V.—THE INCIDENCE OF COMPLICATIONS IN THE UNTREATED SERIES.

Case Number.	Day of Disease on Admission.	Total Febrile Period (Days).	Complications.	Results.
20B	14	31	Slight hæmorrhage	Recovery
21B	7	36	Hæmorrhage	Recovery
22B	27	50	Severe hæmorrhage	Recovery
23B	8	78	Slight hæmorrhage, generalized furunculosis (*Staphylococcus aureus*)	Recovery
24B	14	38	*Otitis media*	Recovery
25B	8	43	*Otitis media*	Recovery
26B	5	89	Thrombosis of the left femoral vein, pulmonary embolism, pyelitis (*Bacillus coli*)	Recovery
27B	13	21	Pneumonia, toxæmia	Death
28B	23	27	Toxæmia (no autopsy)	Death
29B	16	28	Toxæmia, urinary infection (*Bacillus coli*)	Death

Patient No. 21B suffered from exophthalmic goitre.

outcome was obvious that a request to try vaccine treatment as a last resort was made by the physician. At this stage there were signs of a developing pneumonia. A small dose of the vaccine (fifty million) resulted in the patient becoming rational for a couple of hours (the first time for several days), but the pneumonia progressed and despite three other small injections the patient died. *Post mortem* examination revealed extensive double pneumonia. The ulcers in the terminal sixty centimetres of the ileum were all in the stage of healing, the vast majority merely requiring the epithelium to grow over to complete the healing process. Death was undoubtedly due to the pneumonia.

In such a case it is obvious that vaccine therapy directed against *Bacillus typhosus* can do no good, as the typhoid infection has ceased and the secondary invaders are the cause of the trouble. Here again early vaccine therapy, by abolishing the toxæmia of the typhoid infection with its attendant leucopenia, should leave the bone marrow more fit to respond to secondary infections with other organisms, though once such invaders are established, vaccine therapy is of no use to combat them.

The two deaths which occurred among the children treated by this method, were both due to secondary infection. In Case No. 46 (Alfred Hospital series) a bilateral parotitis was observed on the twelfth day and two days later *cancrum oris* developed. Signs of pneumonia appeared and death occurred on the nineteenth day of the illness. In Case No. 53 (Children's Hospital series) an intravenous injection of vaccine was given on the twelfth day of the disease. An excessive reaction followed, the temperature reaching 41.7° C. (107° F.). The toxæmic features of the disease increased and death occurred four days later. Necropsy revealed extensive pneumonic consolidation of the right lung, in the upper lobe, lobar in type, in the lower lobe, broncho-pneumonic. The left lung was congested and œdematous with patchy consolidation. The bowel lesions were in the stage of separation of the sloughs.

The results of the present investigation show that the incidence of complications is not appreciably altered by vaccine therapy. This is also the conclusion of many other observers. The absence of toxæmia in the treated cases removes one of the main causes of death in typhoid fever, but it is only where vaccine therapy is used early in the disease that a lessened incidence of such complications as perforation, hæmorrhage and secondary infections may be expected.

Relapses in the Treated and Untreated Series.

The incidence of relapses in the two series was much the same, the treated cases perhaps being less liable to relapse. Two of the three relapses in these patients were cured by crisis after one more injection, while two injections of vaccine given at an interval of five days failed to affect the pyrexia in the other patient.

To prevent relapses Gay[3] Meyer[4] and Wiltshire[5] all advocate the use of subcutaneous injections of typhoid vaccine after the fever has subsided in response to intravenous therapy.

Besredka's[13] experimental work on the immunization of rabbits against *Bacillus typhosus* infection suggests that relapses may be even more efficiently prevented by giving typhoid vaccine *per os* after the fever has subsided and while the intestinal wall is still abnormal allowing the easy penetration of the vaccine. Two patients who had responded well to one intravenous injection of vaccine on the tenth day of the disease, were given the vaccine daily by mouth before breakfast for several days, the dose

varying from one thousand million to forty thousand million, usually being ten thousand million *Bacillus typhosus*.

In one case the fever recommenced two days later and, despite the daily oral administration of the vaccine, gradually progressed. On the twelfth and fifteenth days of the recrudescence of the fever, intravenous injections of vaccine abolished the commencing toxæmia and caused some diminution of the fever, though there was no crisis. The other patient remained afebrile for six days after the original injection. Though the vaccine had been given daily by the mouth, a relapse then occurred and the fever failed to respond to an intravenous injection of vaccine on the eighth day of the relapse. Both patients eventually recovered.

These two cases are not included in the tables, as the intravenous therapy was complicated by the use of the vaccine by mouth. Undoubtedly both would have done excellently under intensive intravenous vaccine treatment, whereas the results of the oral administration of the vaccine were disappointing.

Detailed Observations on the Vaccine Administration.

The Type of Vaccine.

Two types of vaccine were used in this investigation. A stock vaccine containing *Bacillus typhosus*, *Bacillus paratyphosus A* and *Bacillus paratyphosus B* in the proportions 2:1:1 was used in the seventeen patients of the Alfred Hospital series, in twelve of the Melbourne Hospital patients and in four of those treated at the Children's Hospital.

Nineteen patients received injections of a vaccine of *Bacillus typhosus* only, while in three cases both types of vaccine were used. In the preparation of these vaccines the organisms were grown on beef agar, peptone agar or trypsinized veal agar and were killed by heat or by standing for two or three days in 0.5% carbolized saline solution. The vaccine was always put up in 0.5% carbolized saline solution.

French[6] has suggested that the preparation of the culture medium on which the organisms are grown, is important. It has been found that more definite reactions follow intravenous injection of a vaccine when ox heart has been used instead of horse flesh in preparating the culture media.

The tables do not show any striking difference in the results obtained from the use of the different vaccines. Unless a paratyphoid infection is present nothing seems to be gained by the use of a typhoid-paratyphoid A and B vaccine instead of one of *Bacillus typhosus* only.

Many observers, Gay,[3] Holler[7] and Feistmantel[8] among others, claim that better results follow the use of sensitized typhoidal vaccines. Published reports suggest that the reaction to these vaccines is less severe than that following the use of ordinary vaccines.

The Dosage of the Vaccine.

In adults, the dosage in this series has ranged from fifty to three hundred million *Bacillus typhosus*. At first the larger doses were employed, but latterly it has been found that smaller doses give even better results. The action of the vaccine may be divided into "negative' 'and "positive" phases; the "negative" phase being the period of rigor, rise of temperature, leucopenia and increased malaise, while the "positive" phase occurs with fall of temperature, leucocytosis and abolition of toxæmia. On *a priori* grounds vaccine treatment would fail if the condition of the patient were such that the tissues were incapable of any increased defensive response. In a very toxic patient the excessive stimulation of a large dose of vaccine might conceivably lead to harmful effects by putting an extra load on the already hard worked defensive mechanism of the body. But in the most toxic patients no ill effect has resulted from the use of small doses of the vaccine. In such patients an initial dose of fifty million *Bacillus typhosus* is sufficient and this can be increased according to the reaction of the patient. In the majority of adults a safe initial dose is one hundred and twenty million *Bacillus typhosus*. Large doses (such as two hundred million or more) should be avoided until the patient's response to the smaller amounts has been observed, for the reaction to the same dosage varies greatly in different people. Reference to Tables II. and IV. shows that nothing is usually gained by increasing the dose of vaccine above two hundred million *Bacillus typhosus*. The advantages of the smaller dosage are well illustrated in those patients under personal supervision (Cases 1 to 29) who were treated with typhoid-paratyphoid A and B vaccine. In only three of nine patients who received injections, the maximum dose of which was two hundred million or more of *Bacillus typhosus*, was the disease aborted by crisis. One of these suffered from a relapse which was cured immediately by another injection. In three others the toxæmia was abolished, but the fever persisted unaltered. The remaining three patients suffered from various complications, one dying as a result of perforation of the ileum. On the other hand the three patients who received this vaccine, the maximum dose injected being one hundred and seventy-five million, were all convalescent within five days of the first injection. It is unnecessary in all but exceptional cases for the dose of the vaccine to exceed two hundred million *Bacillus typhosus*. In particular the initial dose should be small, one hundred and twenty million being a sufficient dose with which to commence treatment.

The following history shows that it is only within certain limits that the febrile reaction of the patient is in any way related to the amount of bacterial protein injected.

A boy of fourteen years weighing 32.7 kilograms (five stone, two pounds) was convalescent from a mild attack of typhoid fever. As *Bacillus typhosus* persisted in the fæces, an intravenous injection of typhoid-paratyphoid A and B vaccine was given. By mistake the house surgeon injected eight thousand million *Bacillus typhosus* and four thousand million each of *Bacilli paratyphosi A et B*, about thirty times the maximum adult dose given in this series. As the vein was exposed to give the injection there was no possibility of the eight cubic centimetres of vaccine having escaped into the tissues. Instead of the usual

rigor within an hour, there was a latent period of about four hours. A mild rigor then occurred, the temperature rose to 39.4° C. (103° F.) and gradually returned to normal. The patient was none the worse for the experience.

The administration of so large a dose of vaccine to so small a patient with such little effect is amazing.

The most suitable dosage of the vaccine for children is difficult to determine. Particularly with the younger children (under ten years) it is advisable to use a small initial dose (ten million *Bacillus typhosus*). If necessary this dose may be increased later according to the reaction of the patient.

The Reaction of the Patient to Intravenous Vaccine Therapy.

The intravenous administration of typhoid vaccine leads to a reaction similar to that following the injection of any foreign protein. Within an hour the patient has a violent rigor which may last for more than thirty minutes. During this time the temperature rises rapidly. Usually it remains high for one to six hours and then falls rapidly or gradually, so that in from twelve to thirty-six hours it is subnormal. Here it remains if cure has been effected, otherwise it rises within the next few hours and another injection of vaccine is given. Frequently the patient complains of headache and rarely of generalized bodily pains, both of which yield to Dover's powder. The pulse-rate rises with the temperature, but only very rarely does it reach the neighbourhood of 150 per minute. Slight cyanosis is sometimes noted. Vomiting may follow if the injection is given soon after a meal.

That hyperpyrexial reactions are undesirable, is illustrated in the tables which show that patients whose maximum temperature in any reaction reached 41° C. (105.8° F.) almost invariably made less satisfactory progress than did those whose reactions were less severe. Table IV. shows that in more than half of the patients with complications this temperature had been exceeded in the reaction to vaccine therapy.

Table II. shows that in the Alfred Hospital series (Cases 30 to 40) the maximum temperature recorded in the two patients cured by crisis was less than in any other of these cases. Of the twenty adults under personal supervision (Cases 1 to 20) only three showed fever which persisted for more than a fortnight after treatment commenced. In two of these the temperature following vaccine therapy had been above 41.0° C. (105.8° F). In only three of the remaining seventeen patients whose fever subsided in all but two cases within five days of the first injection, did the temperature exceed this figure in any reaction. Obviously a febrile reaction exceeding 41.0° C. (105.8° F.) after any injection of vaccine is undesirable and preferably it should be less than 40.5° C. (105.0° F.).

In other words a moderate reaction to the vaccine should be elicited.

Details of Administration of the Vaccine.

The technique used in the injection of the vaccine has been described in a previous paper.[10] Evidence has already been produced to show that the vaccines should be administered daily or at least every alternate day if the best results are to be obtained. It has also been shown that it is undesirable to elicit a febrile reaction exceeding 40.5° C. (105.0° F.) after the injection of the vaccine.

Two factors are of importance in this connexion. The first is the dose of the vaccine and as individuals vary in their response to the same amount of vaccine, a small initial dose is advisable (one hundred and twenty million *Bacillus typhosus* for adults). This may later be increased if necessary according to the reaction of the patient. The second factor is the temperature of the patient at the time of the injection. Obviously the higher the temperature before the vaccine is given, the greater is the liability to an excessive febrile reaction. Hence it is advisable to give all vaccines in the early morning before the patient's temperature has commenced its daily rise. Usually the injections were given about 9 a.m.. In the Alfred Hospital series the vaccines were given between 4 p.m. and 8 p.m. Where, despite the early hour, the fever is high, it is advisable to sponge the patient to reduce the temperature to the neighbourhood of 38.3° C. (101° F.) before injecting the vaccine. By these means hyperpyrexial reactions will occur much less frequently.

The earlier in the course of the disease that this treatment is adopted, the better will be the results obtained.

The best routine treatment in the adult consists of an initial dose of about one hundred and twenty million *Bacillus typhosus*, gradually increased if necessary to two hundred million provided the reactions have been mild. The vaccine is repeated daily (usually when the temperature after falling below normal commences to rise again) for about four days, guided by the condition and reaction of the patient. If there is no definite alteration in the fever by this time, little is usually gained by further injections. In most cases the toxæmic features of the diseases will have disappeared and any recurrence of the toxæmia will be abolished by further vaccine therapy. Where the temperature chart has been modified (the pyrexia persisting on a lower scale), further treatment may lead to complete suppression of the fever. With the disappearance of the pyrexia and the toxæmia convalescence commences and only the supervention of complications, especially secondary infections, will occasion any worry. When once the fever has definitely responded to vaccine therapy, any rise of temperature, if it be due to a recrudescence of the typhoid infection, will readily respond to another series of injections. If it be due to secondary infection or some associated disease, the fever will not be satisfactorily influenced by further vaccine treatment.

Both Gay[9] and Galambos[9] who advocate the use of sensitized vaccines, have reached similar conclusions with regard to dosage and frequency of administration of the vaccine.

The Contra-Indications to Vaccine Therapy.

The contra-indications to vaccine therapy are stated by various observers to be as follows: (i.) Hæmorrhage, (ii.) perforation, (iii.) pneumonia,

(iv.) myocardial degeneration, (v.) meningeal symptoms.

It has already been stated that intestinal hæmorrhage was less severe and not more frequent in the treated cases than in the control series. Recent observers incline to the idea that mild hæmorrhage is not a contra-indication to this treatment. This is borne out by the history in Case No. 29. Before being sent to hospital the patient had a moderate hæmorrhage and within twenty-four hours of admission about five hundred cubic centimetres of old blood were passed *per rectum*. Shortly after admission he received two hundred and seventy-five million of *Bacillus typhosus* vaccine intravenously and an excessive reaction followed to 42.0° C. (107.6° F.). Next day no vaccine was given, but on each of the four succeeding days a dose of one hundred and fifty million *Bacilus typhosus* was administered without any untoward result. There was no further hæmorrhage and though the pyrexia persisted, toxæmic manifestations disappeared and recovery was uneventful.

When hæmorrhage is suspected, it is advisable to use small doses of vaccine.

A severe hæmorrhage would be a contra-indication to this method of treatment. The rarity of any indication of a focal reaction after vaccine administration suggests that when it is recorded, it is probably quite independent of vaccine treatment.

Perforation necessitates immediate operation and is a contra-indication to vaccine treatment.

Pneumonia, if *Bacillus typhosus* is the causative organism, is an indication for carefully regulated vaccine therapy. Where secondary invaders are responsible, vaccine treatment is not likely to be of value. In either case the initial dose should be small (fifty million *Bacillus typhosus* for an adult).

Evidence of mild myocardial degeneration is no contra-indication to vaccine therapy as is shown by the history already given in Case No. 15. On the other hand a severe affection of the myocardium would be a contra-indication to vaccine therapy. A small initial dose of vaccine is advisable in any patient whose heart is showing signs of the effects of the toxæmia.

The presence of meningeal symptoms suggests lumbar puncture as a therapeutic measure in addition to careful regulation of the dosage of the vaccine.

The Immunity Response in Intravenous Vaccine Therapy.

In a previous publication[10] evidence was brought forward showing that specific antibodies against *Bacillus typhosus* are produced in great quantity in response to this form of treatment. This is shown by the extraordinarily high titre agglutination curves and the strong complement fixation reactions obtained from the sera of these patients. Korányi[11] found that the opsonic index rises after intravenous therapy, while Inez Smith in Gay's laboratory found that it rose much more in cases abortively cured than those merely benefited by vaccine treatment.

The cellular response after the intravenous administration of vaccines is similar to that which follows the intravenous injection of any foreign protein. The initial rise of temperature is accompanied by a leucopenia and the fall of temperature by a leucocytosis, both resulting mainly from decrease and increase of the polymorpho-nuclear elements. Drinker[12] states that in the rabbit this stage of leucopenia corresponds with a great increase of polymorpho-nuclear cells in the liver and spleen. Living *Bacilli typhosi* injected intravenously are found in these organs within a few minutes of injection synchronously with the change in distribution of the leucocytes. He explains the leucopenia on the basis of a positive chemiotaxis, while the leucocytosis results from the discharge from the internal organs of the accumulated leucocytes together with new cells from the bone marrow.

The Mechanism by Which Beneficial Results are Obtained in Intravenous Vaccine Therapy.

It has been shown that there is both a cellular and a humoral response to this form of treatment and while orthodox views regarding immunity reactions are held, it is impossible to accept fully any theory suggesting that the good results of this treatment are quite independent of a specific immunity response.

Besredka's[13] recent work has, however, seriously challenged the view that the so-called specific antibodies play any great part in the true and lasting immunity which results from an attack of typhoid fever. He holds that these antibodies are merely concomitant effects of the infection due to overflow of typhoidal protein into the blood stream. By the oral administration of typhoid vaccine,, he succeeded in protecting rabbits against intravenous inoculation with a usually fatal dose of living typhoid bacilli. In some of these animals with a very high grade of immunity no antibody could be detected in the blood. It is suggested that the general immunity to infection with *Bacillus typhosus* is really dependent on a local intestinal immunity whereby certain "receptive" cells in the mucosa of the small intestine with a special affinity for *Bacillus typhosus* become capable of digesting increasingly large amounts of the virus. Only when the infection is excessive do the bacilli overflow the receptor apparatus and become disseminated. On this theory intravenous therapy acts by stimulating the local receptor apparatus of the intestine causing a local immunity in addititn to the production of specific antibodies to the typhoidal protein injected into the blood stream.

It would appear that the administration of typhoid vaccine *per os* might prove useful in the treatment of typhoid fever. It has already been stated that in two patients who had temporarily responded well to intravenous therapy, the oral administration of vaccine gave disappointing results. One other patient who was moderately ill, was given daily doses of typhoid-paratyphoid vaccine by mouth from the tenth to the thirteenth day of her illness, the doses ranging from one thousand million to five thousand million *Bacilus typhosus* with half this amount of both *Bacilli paratyphosi A et B*. The only sign of any improvement was shown in the tongue which had previously been dry except at the tip and edges. Within twenty-

four hours of commencing this treatment the tongue was clean and moist. Otherwise there was no apparent difference in the patient's condition and the fever subsided on the thirty-third day.

Various observers, Kraus,[14] Lucksh,[15] Holler[16] and Reibmayr[17] among others, have found that different substances, such as vaccines of *Bacillus typhosus, Bacillus coli* and *Vibrio choleræ* as well as proteoses, colloidal metals and sodium nucleinate given intravenously in typhoid fever all lead to the same type of reaction with beneficial results.

Starkenstein[18] and von den Velden[19] both observed alteration in the permeability of the capillary wall after intravenous therapy. There is increased permeability in the stage of malaise and fever, while the subsidence of the toxæmic features of the disease is accompanied by a period of diminished permeability of the capillaries.

Numerous factors both of non-specific and of specific origin are probably concerned in the production of the beneficial results of this form of treatment. As the use of vaccines of *Bacillus typhosus* intravenously leads to both specific and non-specific types of reaction, it seems advisable to employ them in preference to other forms of protein in the treatment of typhoid fever.

The Dangers of Intravenous Therapy in Typhoid Fever.

In this series of cases, despite the injection of larger doses of vaccine than are here advocated, no untoward results directly attributable to the use of the vaccine have occurred.

From the literature it is obvious that thousands of injections of typhoid vaccine have been given intravenously in typhoid fever with very few harmful effects. With careful dosage the risk of any untoward result is remote. Miller[20] mentions that *delirium tremens* may develope in a confirmed alcoholic after the intravenous injection of typhoid vaccine. Gay[3] remarks that the few individuals who remain unconvinced of the value of intravenous vaccine therapy in typhoid fever or who are unwilling to risk the very rare harmful effects following the injection, have based their opinion on very few cases.

Conclusions.

1. The intravenous administration of typhoid vaccine in appropriate doses is of great value in the treatment of typhoid fever. It does not replace the routine treatment of this infection, but it is a very important addition to our therapeutic armamentarium.

2. With care in dosage neither excessive febrile nor focal reactions need be feared. Large initial doses of the vaccine must be avoided. A febrile reaction exceeding 40.5°C. (105° F.) is inadvisable. Focal reactions so rarely follow these injections that when they do occur, they are probably quite independent of vaccine treatment.

3. The best routine treatment in an ordinary uncomplicated case of typhoid fever in adults consists in the daily administration for three or four days of a polyvalent vaccine of *Bacillus typhosus* as soon as the diagnosis has been made. The initial dose should be about one hundred and twenty million *Bacillus typhosus* and this may be gradually increased to two hundred million if necessary. In young children it is advisable to use a small initial dose (about ten million). This may be increased later according to the reaction of the patient.

4. Perforation, severe hæmorrhage, severe myocardial degeneration and severe secondary infection are contra-indications to vaccine therapy. Mild hæmorrhage, pneumonia, mild myocardial degeneration, meningeal symptoms and severe toxæmia are indications for the use of smaller doses of vaccine than usual.

5. Unless used early in the disease, vaccine therapy has little influence on the incidence of complications in typhoid fever.

6. Intravenous vaccine therapy in typhoid fever leads to:

(i.) The dramatic termination of the fever by crisis in many patients;

(ii.) The diminution or abolition of the toxæmic features of the disease in the majority of uncomplicated cases.

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Reports of Cases.

PRIMARY BLASTO-MYCOTIC MENINGITIS OCCURRING IN A CHILD.

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THE first case of blasto-mycotic meningitis reported in Australia and apparently the first reported instance in which the disease appeared primarily in the meniges was recorded by Swift and Bull in THE MEDICAL JOURNAL OF AUSTRALIA during 1917.(1)

Since that time Williams has recorded a case in which meningitis followed pulmonary blasto-mycosis(3) and Badham has mentioned the occurrence of a case in Sydney during the year 1922.(4)

The case herein recorded is of special interest by reason of its occurrence in a child and in being as far as I can ascertain the second case on record of primary blasto-mycotic meningitis.

A dog was infected by intrathecal injection of cerebro-spinal fluid from the child and a blasto-mycotic meningo-myelitis ensued and ran a rapid course to a fatal issue.

The mode of infection in the primary human cases remains undetermined and there was nothing in this case to suggest a route of entry of the parasite.

Watanabi(2) has reported a case of blasto-mycotic meningitis in which blasto-mycotis invasion of the tonsils was found; this he regarded as the primary focus.

In the case reported here no disease of the tonsils was detected.

The same writer speaks on two other cases and says that in none of the three was there any blasto-mycotic infection of the lungs.

CLINICAL NOTES.

T.R., a female, *ætatis* three years and three months, was admitted to hospital on February 21, 1922, with a history of four weeks' illness.

Symptoms commenced with looseness of the bowels for about a week, the motions being green but without blood or mucus; then restlessness became noticeable alternating with a drowsy condition, in which, however, the child would answer if spoken to. Her condition remained the same until she was taken to hospital. She continued to be restless, grinding the teeth and crying out at intervals, sometimes putting the hand up to the face. She would only eat after considerable persuasion. The bowels became constipated and she would sometimes cry before passing water. For seven days before admission to hospital she appeared unable to sit up and cried if she were held in a sitting position, but she could still use all the limbs freely.

The past history was that the child had always been healthy and apparently normal. She had had a fall on the head fourteen months before the illness commenced, but this was apparently trivial. About two months before the onset of this illness the child was treated for pain on micturition; at that time she appeared rather quiet and not quite herself. The family history revealed nothing of importance.

On arriving at hospital the child lay in bed with its eyes closed and grinding its teeth at intervals. At times it would put the hands to the head and cry out. It was very irritable and would cry if touched, but appeared to be only semi-conscious. The left side of the face showed muscular twitching and the pupils were equal and moderately dilated. She appeared to be able to move all the limbs. There was no head retraction, but the neck was somewhat stiff and Kernig's sign was present, also a *tache cérébrale*. The superficial abdominal reflexes were active and the plantar reflexes flexor; the knee-jerks could not be elicited. The temperature was 38.9° C. (102° F.) and the pulse-rate 120.

Lumbar puncture was performed and thirty cubic centimetres of clear fluid were drawn off, as there was considerable increase in pressure. A moderate number of lymphocytes and large mononuclear cells were present and the fluid gave a definite globulin reaction, but no micro-organisms were detected by direct examination or culture.

Nothing abnormal was made out in the examination of the lungs or heart. The retinæ could not be satisfactorily examined on account of the child's restlessness.

For the next few days the child's mental condition varied; at times she was drowsy and would not answer questions; at others she would answer more or less intelligently and at others she would laugh and cry.

On February 24, 1922, lumbar puncture was again carried out and the fluid was almost clear. The same pathological findings were recorded as before.

Lumbar puncture was repeated at about two day intervals and usually about thirty cubic centimetres of clear fluid were drawn off.

During the month of March the general condition appeared to improve for a time and the mental condition was better, but subsequently she became worse, lying curled up in bed with her limbs and back stiff.

Red blood cells were noticed in the spinal fluid during the latter half of March, being usually somewhat more numerous than the lymphocytes.

On April 5 the spinal fluid was semi-opaque with a yellowish amorphous material; numerous yeast cells were discovered in addition to lymphocytes. Subsequent specimens of fluid contained progressively less of the yellowish matter, but yeast cells remained abundant until the child's death.

At about this time it was observed that the child appeared to have lost its sight and subsequently Dr. Edgar Brown reported that there was primary optic atrophy on both sides.

The drowsiness increased and gradually the child became almost continually unconscious. She was greatly emaciated and died on May 22, 1922, that is, three months after admission.

The temperature chart showed almost regularly an evening rise with morning remission to almost normal. After the first day in hospital the temperature did not go appreciably above 37.8° C. (100° F.), until April when it began to reach 38.9° C. (102° F.) and sometimes 39.5° C. (103° F.), but for a few days before death the temperature was subnormal.

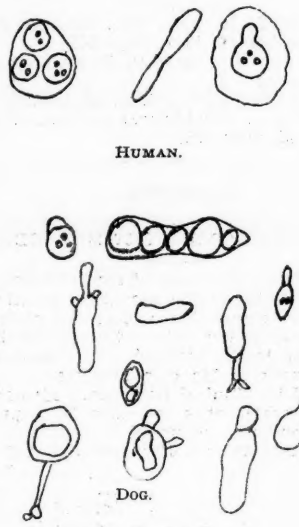

FIGURE I.

PATHOLOGICAL REPORT.

The body was very wasted and the limbs in the position of general flexion.

There was some excess of somewhat turbid cerebro-spinal fluid at the base of the brain and in the spinal theca.

The *pia mater* appeared thickened and somewhat gelatinous, with areas of brownish pigmentation especially about the medulla and spinal cord.

Macroscopic section of the brain and spinal cord showed little beyond a moderate thickening of the *pia mater*.

There was mottling of the lungs posteriorly due to scattered areas of broncho-pneumonia. There were no signs of the gelatinous infiltration described as characterizing pulmonary blasto-mycosis nor were any signs of tuberculosis detected in the lungs or bronchial glands.

No abnormality was seen in the heart beyond pallor of the myocardium.

Nothing abnormal was found in the abdomen.

The bones were examined as far as possible for signs of disease, but none were found.

Radiographic examination of the bones was made during life to determine the presence of any disease focus.

Microscopical Examination.

Brain.

The *pia mater* was œdematous and infiltrated with round cells. This infiltration was patchy and nowhere very extensive. Yeast cells were present chiefly between the *pia* and the brain, but some in the interstices of the *pia*. The forms present are depicted in the rough sketch reproduced (see Figure I.).

There were moderately thick sheaths of round cells surrounding the vessels as they passed into and out of the brain.

Spinal Cord.

The changes here were similar to those in the brain, but rather more marked. The cellular infiltration was denser and more yeast cells were present. These, however, were not detected anywhere within the actual nervous tissues.

Lungs.

The greater part was practically normal. The darker areas posteriorly showed vascular congestion and accumulation of cells within the alveoli, in some instances practically filling them. No signs of blasto-mycotic invasion were found anywhere.

THE PARASITE.

The appearance of the parasite in the cerebro-spinal fluid obtained at puncture was that of a yeast-cell, often budding, with a rather thick envelope, surrounded by an irregular capsule which could only be made out with difficulty. Each cell contained one or more highly refractile, rounded bodies. Usually they were two or three in number and occurred in the central part of the cell.

Various other forms occurred in addition to the spherical and budding forms, especially in a dog which was infected and will be referred to later.

Cultural Reactions.

Growth was originally obtained most readily on egg-medium, but also on Löffler's serum. On the egg-medium the colonies were visible on the fourth day of incubation as almost transparent dots. In a few days' time the colonies appeared as smooth drop-like projections from the surface of the medium.

Subcultures from these colonies grew on agar as well as in broth (glucose), but these were not luxuriant. After subculturing several times on egg-medium a luxuriant growth was readily obtained on agar especially glucose agar, but in broth the growth was still somewhat scanty. Growth occurred in glucose, mannite and lactose with acid formation in glucose, but in the latter two the growth was too scanty to draw conclusions as to the power of the parasite to split the sugars.

Animal Inoculations.

With the aid of Mr., now Dr., West, a spinal puncture was performed in the lumbar region of a fox-terrier and about three cubic centimetres of fresh cerebro-spinal fluid from the child were injected.

Next day the dog was very quiet and had a slight limp in the left leg.

The dog became progressively quieter and more ill looking, never barking and only occasionally whining a little. The weakness in the leg increased and the other limb became affected until, ultimately, after twelve days the hind limbs were unable to support the animal. Mus-

FIGURE II.
Dog's Spinal Cord; Infiltration with Blasto-mycosis—Microscopical Section.

cular tremors were noted at about this time, affecting the whole body and the animal had by now become greatly emaciated and looked very miserable. It had not taken food properly since the injection and now scarcely touched anything.

On the fourteenth day the animal became unconscious and was then killed by chloroform.

The brain and cord were removed for detailed examination. The other organs showed no gross abnormalities.

Brain and Spinal Cord.

There was much thickening of the *pia mater* especially over the lower half of the cord. The appearance was that of a gelatinous membrane.

On sectioning the cord, the *pia mater* was seen to be thickened to the extent of one millimetre over a large part of the circumference of the cord. In addition, a somewhat triangular area of infiltration having a semi-transparent gelatinous appearance, was seen in the cord approximately the size of an eighth of the cross section and lying posteriorly with its base at the circumference of the cord on the right side. The infiltrated area in the cord was traceable upwards to the dorsal region where it became progressibly smaller and disappeared in the lower cervical region.

On microscopical examination unstained sections of the cord revealed very great numbers of yeast cells, many of the type seen in the human cerebro-spinal fluid, but in addition the forms depicted in Figure I. These occurred both beneath the *dura mater* and also in the infiltrated areas of the cord and in the thickened *pia mater*.

Stained sections showed extensive areas of degeneration of the nervous elements with inflammatory infiltration. The *pia mater* was thickened in all parts of the lumbar and dorsal regions and beneath it was a thick zone of inflammatory cells corresponding to the affected area seen macroscopically. The cells were chiefly lymphocytes with some plasma cells and a few multinuclear cells, as well as a few young connective tissue cells.

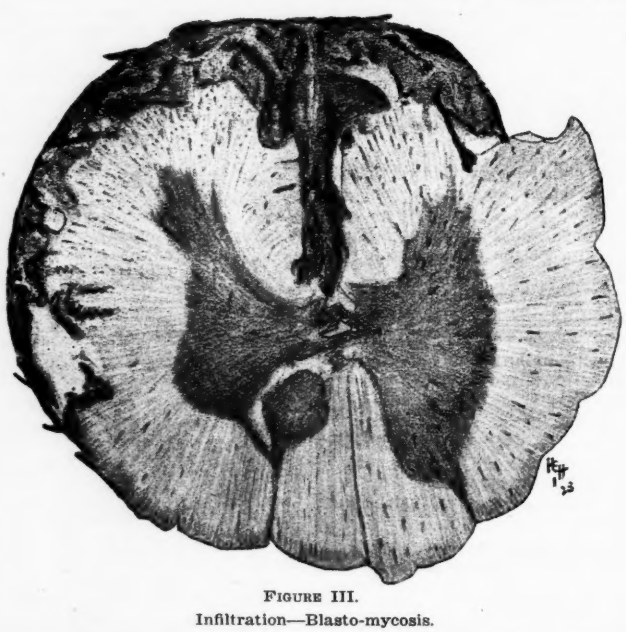

FIGURE III.

Infiltration—Blasto-mycosis.

Occasionally one of the larger cells was found to contain a yeast cell. There were small spaces in the infiltrated areas and also a larger space in the triangular area previously mentioned. In these spaces yeast cells were very numerous.

The infiltration extended into a considerable portion of the posterior horn of the spinal grey matter on the right side. Figure III. depicts a section of the cord.

Subcutaneous inoculation of a guinea pig did not lead to a blasto-mycotic infection. The parasite appears to correspond closely to those found in the other Australian cases.

Acknowledgments.

Dr. Gunson, Senior Honorary Physician to the Adelaide Children's Hospital, has kindly allowed me to use the clinical notes of the case.

Mr. Hosking, sixth year medical student, has taken much care in preparing a micro-photograph and sketch of the dog's cord.

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Reviews.

CLINICAL LABORATORY METHODS.

IN these days, when the work of the laboratory is becoming such a vital factor in the successful practice of medicine, a manual containing clear and precise directions as to the method of carrying out tests and procedure, becomes an absolute necessity to the medical practitioner who is endeavouring to work in his own laboratory.

Such a manual is "Clinical Laboratory Methods," by Dr. Russell Haden,[1] which has recently been published in America. The particular value of this book is that only tried and tested methods are discussed and that practically only one method is given for each quantitative determination when one method is adequate. As far as possible, only such procedures are suggested as may be carried out in any moderately well-equipped laboratory.

In the first chapters the author deals with urine examinations; the colorimetric methods of Folin are much in evidence in this as well as in the chapters on blood chemistry. To anyone who desires to use colorimetric methods, it may be said at once that this book will serve as a very useful and reliable guide, as details of methods of estimating such contents as urea, glucose, total nitrogen, ammonia, uric acid, creatinine and the various salts, whether in urine or blood, are fully described.

Methods of gastric analysis and examination of fæces are dealt with and there are chapters on serological technique and bacteriological methods.

The use of the colorimeter is explained and adequate space is devoted to general laboratory technique.

The book is well printed on good paper and is illustrated by several coloured plates and a great many line blocks of a special apparatus with the methods of using them. Full details are given as to the preparation of all necessary reagents and in every instance the authority for the particular test is quoted with the reference to journal, pamphlet or manual from which the test has been extracted.

As it is impossible for the practitioner to keep in touch with all the modern scientific and chemical journals, such a book as this which culls the best of the new methods of analysis and shows how to use them, becomes of the utmost value. We can confidently recommend it to anyone who is contemplating the establishment of a laboratory for the purpose of utilizing the modern methods of bio-chemical or bacteriological investigation into disease processes.

[1] "Clinical Laboratory Methods," by Russell Landram Haden, M.A., M.D.; 1923. St. Louis: C. V. Mosby Company; Demy 8vo., pp. 294, with five coloured plates and 69 illustrations in the text. Price: $3.75.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 22, 1923.

Death of Sir Walter Davidson.

THE grief of the whole community at the sudden death on September 16, 1923, of His Majesty's representative, His Excellency Sir Walter Davidson, is shared by the medical profession throughout the Commonwealth. Apart from the serious loss sustained by the people through the death of so admirable and so popular a Governor, the scientific world has been deprived of a staunch and able supporter who has always brought sympathy and understanding to those in search of Truth.

The Depopulation of the Pacific.

AT the Pan-Pacific Science Congress recently held in Melbourne and Sydney the leaders in hygiene in the countries bordering on the Pacific and a few from more distant lands endeavoured to analyse the causes that are operating in the diminution of the native races of the Pacific Ocean. A summary of the debate will be published in an early issue. From it will be seen that those who have studied this question, have come to the conclusion that disease, social causes and political action are responsible for the unmistakeable deterioration of these interesting and by no means unintelligent peoples. The political influences need not be discussed in this place, since the opinions on political matters held by members of the medical profession embrace all schools of political thought. The social influences are complex and often indirect. History has produced many instances of the ill-effects of so-called civilization on native races. It is well-nigh impossible for the Melanesian and the Polynesian to adopt the customs and habits of the west without manifesting undoubted deterioration. Those who have watched the result of some of the innovations, are unanimously of opinion that European clothing does not suit the Pacific islanders. Not only do they fail to understand that this form of clothing must be changed when wetted by rain, but it is evident that the native covering is much more hygienic and for these children of Nature, at all events, much more conducive to moral behaviour. The European house, too, tends to emphasize any inherent unhygienic habits and in the tropical islands is both unnecessary and harmful. There is a grave question whether contact with the white man is not in itself a baneful influence for the native islander. At all events it would seem as though this contact had led to deterioration in habits and customs and perhaps in ethics as well. The suggestion has been put forward that intertribal warfare and the uncertainty of life has had the effect of reducing the male part of the population of the islands as compared with the female. The maintenance of a numerical superiority of the female element in Nature seems to be necessary for the preservation of the virility and strength of the stock. According to this view the interference of the white man in the domestic quarrels of the native has led to a survival of too large a preponderance of males, with the result that the races tend to deteriorate.

Whatever may be the decision in regard to the influences which the white man has exercised on the social and ethical lives of the native islanders, there can be no doubt that in the last instance disease is the actual cause of the racial decay. Not long ago we published a full summary of the researches carried out by Dr. F. W. O'Connor in the Ellice Islands and in Samoa on behalf of the London School of Tropical Medicine. In his report he gave a formidable list of diseases encountered among the natives of these islands. Tuberculosis is perhaps the most important. It is very deadly when sown on the susceptible soil of the Pacific natives and its toll is alarming. Filariasis and framboesia are serious infections which leave indelible marks in their trail. Intestinal infestations by hookworm and other helminths and intestinal infections have become common, while occasional epidemic outbreaks spread like a bush fire through a sun-baked country among the natives. Dr. J. H. L. Cumpston pointed out that the fundamental defect lay in the absence of an immunity to the common diseases of white races.

The establishment of a Pacific Medical Service to investigate the incidence and causes of disease among the inhabitants of Pacific islands has been advocated on many occasions in these columns. The Pan-Pacific Science Congress passed a resolution to the effect that the preservation of the health and life of the native races was the scientific problem of the Pacific that stands first in order of urgency. Dr. Cumpston suggested that the International Health Board would be the best organization to undertake the work and he intimated further that the centre of the scheme should be placed in Townsville. Under the conditions of financial stringency it is obvious that a Pacific Medical Service could not be organized and maintained at present either by the Commonwealth or by the Imperial Government. Perhaps the most ideal arrangement would have been the establishment of this service by the Commonwealth Government with the collaboration of all countries with Pacific possessions. It is questionable, however, whether such a scheme of collaboration would be workable. The proposal put forward by Dr. Cumpston is both practicable and wise. The International Health Board of the Rockefeller Foundation has earned the recognition, respect and admiration of the whole world for the wonderful international work it has accomplished. In Australia it has achieved very much. The Australian Hookworm Campaign owes its existence to the International Health Board and it has now become an established service of the greatest value to the community. The activities of the Commonwealth Department of Health in connexion with industrial hygiene, with laboratory service and with modern sanitary science have been initiated with the aid of experts in these special subjects from the International Health Board. In Great Britain the Board has done even more for the public weal. In these circumstances it may be stated without fear of contradiction that no other organization in the world is better fitted from every point of view for the task. The International Health Board attacks a problem by taking a survey of the work to be done and by forging the weapons wherewith the work can be expeditiously and effectively accomplished. The Board, moreover, always seeks the collaboration of the workers in the country to which its experts are sent. It is truly international. We may express the hope that before long we shall have a Pacific Medical Service working earnestly to stem the tide of destruction which threatens to engulf the native islanders of the Pacific.

Current Comment.

INTRA-CRANIAL ANEURYSMS.

SURPRISINGLY little has been written by the authors of text-books of medicine on the subject of intra-cranial aneurysms. The recognition of the condition during the life of the patient is unusual and in *post mortem* examinations the presence of much blood clot in the meshes of the *pia mater* may so obscure the picture that, unless careful search is made for the aneurysm, it is liable to be missed. Intra-cranial aneurysms occur in males more often than in females and are said to be equally as common before as after forty years of age. It has long been recognized that they may be associated with infective endocarditis. Embolism without complete occlusion of the vessel may occasion an injury to the vessel wall and so be the cause of aneurysm. Arterial degeneration may be an antecedent factor and trauma, especially affecting the internal carotid artery, may give rise to an aneurysmal dilatation. Many observers have attributed to syphilis a share in the ætiology. Fearnsides and Turnbull independently of one another recorded observations from which they concluded that this was not as frequent as had previously been supposed. They held that the association was exceedingly rare. They thought that there was sufficient evidence to justify the conclusion that in some instances a congenital factor entered into the causation.

Dr. C. P. Symonds has recently studied the condition from a clinical standpoint.[1] He refers to the work of William Gull who recognized the comparative frequency of the condition in 1869. Dr. Symonds records the histories of five patients in regard to whose condition a diagnosis of intra-cranial aneurysm was made. The diagnosis was confirmed at autopsy in three instances. The other two patients were alive at the time of reporting. The first patient of the series was seen by Dr. Symonds at the clinic of Professor Harvey Cushing in 1920. The clinical picture was characterized by alternating periods of consciousness and unconsciousness. Pain was present and sub-retinal accumulations of blood were found on examining the *fundus oculi*. A sub-tentorial decompression operation was performed by Professor Harvey Cushing and much extravasated blood was found on opening the *dura mater*. At the autopsy a small saccular aneurysm was found at the junction of the right internal carotid and posterior communicating arteries. The clinical histories of the other two patients who died, were somewhat similar. In one

[1] *Guy's Hospital Reports*. April, 1923.

patient there occurred a return to consciousness within a few hours of death. Dr. Symonds regards this feature as of diagnostic value in differentiating the lesion from an intra-cerebral hæmorrhage. He also states that the appearance of pain and rigidity in the neck shortly after an apoplectic seizure should arouse the suspicion of sub-arachnoid rather than intra-cerebral hæmorrhage. In two of the patients submitted to lumbar puncture blood was found in the cerebro-spinal fluid.

Dr. Symonds divides the signs produced by an intra-cranial aneurysm into neighbourhood signs, signs of the disease such as arterio-sclerosis or infective endocarditis which may be associated with the lesion, and signs of leakage from the sac. The signs of leakage from the sac are those which enable the diagnosis to be made with a reasonable certainty.

Professor Harvey Cushing has discussed the subject of intra-cranial aneurysms from the point of view of the surgeon.[1] He states that patients admitted to the surgical wards of a hospital for symptoms which have suggested the presence of an intra-cranial tumour, may be divided into those with undoubted tumours and those with suspected tumours. He points out that the tumour "suspects" constitute a group presenting great difficulties of diagnosis. The conditions met with in this group include chronic arachnoiditis, encephalitis, arterio-sclerosis, nephritis, syphilis, tuberculosis, epilepsy, cephalalgia and a great group of ophthalmic disorders. He records the history of two patients who suffered from aneurysm and presented none of the symptoms described by Dr. Symonds. One patient died before the aneurysm ruptured and the other died after the rupture of an aneurysm which had been mistaken some time previously for a glioma at an exploratory operation. He also records the fact that four patients presenting typical symptoms were thought to be suffering from hæmorrhagic pachymeningitis, *ophthalmoplegia externa*, ophthalmoplegic migraine and a tumour of the trigeminal nerve sheath. He lays stress on the fact that hypertension and arterio-sclerosis need not characterize the clinical picture, for many of the lesions occur in comparative youth and are undoubtedly of mycotic origin. Professor Harvey Cushing concludes with the statement that the diagnosis of intra-cranial aneurysm during life must depend on a thorough knowledge of normal and pathological anatomy in addition to clinical acumen.

METASTATIC TUMOURS OF BONE.

IN our issue of February 23, 1923, we drew attention to the subject of metastatic deposits of carcinomata in bone. The two theories of mode of spread were discussed and the views of Sampson Handley, the protagonist of the permeation theory, were ranged ranged alongside those of Piney who in adherence to von Recklinghausen's doctrine sought to prove the accuracy of the theory of spread by the blood stream. The question has been reopened by Dr. Cecil Joll.[1] He states that in order to prove the spread by the lymph stream it is necessary to have a knowledge of the lymphatics of bone and periosteum as well as of the bone marrow. The observations of Piney and his inability to demonstrate the extension of lymphatic channels beyond the periosteum of bone must cast a doubt on the views held by Handley. He states that in order to substantiate the claims made by the supporters of the blood stream theory it is necessary that malignant emboli circulate in the blood stream, that such emboli are able to gain access to the systemic circulation and that these emboli can gain lodgement in the blood vessels of the bone marrow. It will be remembered that one of the two main observations on which Piney based his arguments, was the fact that he had found red blood corpuscles and cancer cells in the same channels in the bone marrow. The communication of malignant masses of tissue with the venous system has also been demonstrated. A ready channel of communication exists by way of the thoracic duct for particles to be transferred from the lymphatic to the venous circulation and it has been shown that portions of the chorionic villi may be shed into the blood stream in eclampsia. Dr. Joll makes reference to the finding of Goldmann that malignant cells reach the blood stream by entering the lumina of small vessels, especially the veins, by way of the *vasa vasorum*. In regard to the means by which the cancer cell gains access to the systemic circulation he refers to the work of Schmidt in the same way as Piney. Schmidt found minute malignant emboli in many instances in the pulmonary arterioles in the interior of thrombi without any evidence of metastasis in other parts of the body. Dr. Joll states that it would follow from Piney's claims that all bone metastases should be found in the red marrow. Piney was able to demonstrate foci of red marrow in the substance of the fatty marrow in addition to that persisting in the upper ends of the humerus and femur. Dr. Joll holds that the specimens described in his paper provide a general confirmation of the contention that the location of metastases and the distribution of the red marrow are interdependent. He also apparently accepts the views of Piney in regard to the formation of new areas of red marrow as a result of the constitutional disturbance of the disease in order to explain the exceptions to this generalization. He points out that observers who have made systematic examinations of the skeleton by sectioning the bones, have found that bones frequently regarded as immune may contain minute secondary deposits in the marrow. This is in his opinion an additional reason for rejecting the lymphatic permeation theory.

Dr. Joll concludes that the weight of evidence is in favour of the theory of transmission by the blood stream and lodgement in the bone marrow. Otherwise it is impossible to explain such an occurrence as a metastasis in the humerus from a primary growth in the rectum.

[1] *Guy's Hospital Reports*, April, 1923.

[1] *The British Journal of Surgery*, July, 1923.

Abstracts from Current Medical Literature.

THERAPEUTICS.

"Insulin" in Diabetics.

ELLIOTT P. JOSLIN (*The Journal of the American Medical Association*, June 2, 1923) states that diabetes, though subdued, is not conquered. "Insulin" is not a cure, nor does it allow a diabetic to give free range to his appetite. All those measures which have proved of the greatest value in the treatment of diabetes without "Insulin," should be simultaneously employed. The diabetic diet must be thoroughly learned and used. If the diet overbalances the drug, there will be free glycosuria and failure of treatment. If the drug overbalances the diet, a reaction, often fraught with alarm, may result. An over-dose of "Insulin" causes a warning train of symptoms, beginning with nervousness and extreme hunger as the blood sugar drops below 0.07%, progressing to sweating and tremor and ending with unconsciousness as the blood sugar reaches 0.03%, when death is a possible result. Recovery, however, follows the simplest of measures—the juice of an orange or from one to three teaspoonfuls of sugar—and takes place promptly within five or ten minutes. Recovery may be further expedited by the subcutaneous administration of one cubic centimetre of a 1 in 1,000 solution of adrenalin, though this also should be followed by the orange or sugar. The treatment of diabetic coma with the drug is spectacular, but coma is an accident and like all accidents is to be avoided. He teaches his patients when ill from any cause to go to bed, to keep warm, to take a glass of hot water, tea, broth, orange juice or oatmeal water gruel every hour, to empty the bowels with an enema and to consult a medical practitioner who, if signs of acidosis present themselves, will probably give "Insulin," digitalis and caffein and wash out the patient's stomach. In coma "Insulin" is best given in doses of ten units every hour for two to four doses and then every other hour for four doses more if necessary. The blood sugar percentage and the urinary sugar are the best guides to the degree of treatment. To some patients with coma it may be safer to give five or ten grammes of carbo-hydrate by mouth to offset the "Insulin" and some of the most successfully treated patients have received fifteen to thirty grammes of sodium bicarbonate. Details of diets for diabetic patients and of the amount of "Insulin" to be administered are also given.

Intra-Cardial Injection of Adrenalin.

CARL BODON (*The Lancet*, March 24, 1923) records the resuscitation of a patient apparently dead by means of an intra-cardiac injection of adrenalin. The author is of opinion that the disease from which the patient was suffering was extreme coronary stenosis caused by syphilis. The condition had not been treated with the usual anti-syphilitic remedies. The patient had a sudden attack of dyspnœa and collapsed. Morphine, camphor oil, ether, caffeine and adrenalin had been in turn injected under the skin or into the muscles without effect. The patient gradually became relaxed and apparently lifeless, the cyanosis of lips and skin gave place to a death-like pallor, the eyes were widely open and the pupils largely dilated, the corneal reflexes were absent and there was complete loss of consciousness. Respiration became irregular and infrequent and then ceased. Fæces and urine were passed involuntarily and the heart ceased to beat. One milligramme (one cubic centimetre of a one in 1,000 solution) of adrenalin was, as a forlorn hope, injected into the right ventricle. A few seconds later the heart resumed its beat, becoming regular and effective in less than half a minute. Within three-quarters of a minute respiration set in with inspirations which became progressively deeper and more regular. Some minutes later the corneal reflexes returned and the widely dilated pupils contracted. The respirations then became deep and snoring and the patient was apparently in a profound sleep. Two and a half hours after the injection he walked to his bed with assistance. This incident happened on May 28, 1922, and the patient has since remained in apparently excellent health. He is at present undergoing anti-syphilitic treatment.

The Efficacy of Arsenic "Antidote."

H. MCGUIGAN, H. V. ATKINSON AND G. A. BROUGH (*The Journal of Pharmacology and Experimental Therapeutics*, April, 1923) agree with De Busscher that the arsenic "antidote" of the United States Pharmacopœia, *ferri hydroxidum cum magnesia oxido*, is of no practical value in the treatment of arsenical poisoning. It has no influence on the symptoms due to the administration of *liquor arsenicalis* in poisonous doses. When arsenious oxide is the poison used in experiments on animals, there is a slight unimportant delay in the onset of death. This they attribute to the colloidal nature of the antidote and to delayed absorption rather than to chemical neutralization.

Liquid Paraffin.

H. B. RUSSELL AND P. C. BRETT (*The Lancet*, March 24, 1923) state that the preparations of liquid paraffin universally obtainable, although probably answering the tests of the British Pharmacopœia, differ widely in viscosity. They made extensive clinical trials with samples whose viscosity varied widely, namely from two hundred and ninety-six to seventy-one. Advantage is taken of the lubricant action of liquid paraffin in its general use as a laxative and lubrication is only ideal when the lubricant is intimately mixed with the fæces. It was found that paraffin of high viscosity had a slightly greater laxative action than one of low viscosity and that when the viscosity was low the mixing of the paraffin with the stool was very imperfect. The authors urge that a viscosity standard of not less than one hundred and eighty should be adopted.

The Biological Assay of Pituitary Extract.

ERWIN E. NELSON (*The Journal of Laboratory and Clinical Medicine*, February, 1923) has pointed out that the so-called "biological assay" methods in general use for the standardization of pituitary extract are unsatisfactory and as a result the variability in oxytocic (labour-hastening) potency of different samples of the extract is considerable. Until exact chemical assay of the drug becomes possible, biological assay methods must be used, but potassium chloride and histamine are not suitable substances for the standardization of pituitary extract. As there is evidence that the oxytocic and pressor substances in the gland are not identical, the pressor method should not be employed in the assay of a drug whose chief use lies in its oxytocic action. There is a lack of parallelism in the oxytocic potency of either potassium chloride or histamine and that of a good sample of pituitary extract. Moreover, histamine is hyogroscopic in nature and is unstable under ordinary conditions of use. It is maintained that a pituitary extract would make a more reliable standard and would insure the preparation of extracts of uniform potency for the use of the medical profession.

Nicotine.

J. P. BAUMBERGER (*The Journal of Pharmacology and Experimental Therapeutics*, February, 1923) publishes the results of an investigation into the nicotine content of tobacco smoke. Cigarettes and cigars were lighted and the smoke puffed mechanically through an apparatus designed to absorb the nicotine in the smoke. It was found that 40% of the nicotine in tobacco appeared in the smoke puffed and this was equivalent to about 0.8% of the weight of the tobacco smoked. A number of different brands of cigarettes were tested and the results were compared with those of previous investigators and found to be in close approximation. The author states that the rate of puffing the cigarette, cigar or pipe would determine the nicotine dosage for the smoker. Frequent puffing would mean increased dose. About 66.7% of the smoke and presumably of the nicotine drawn into the mouth is absorbed. If the smoke is inhaled, about 88.2% is absorbed. Expectoration lowers this figure considerably as the saliva absorbs both smoke and nicotine. The maximum absorption of puffing five times per minute would be 27.5 milligrammes per hour. This dose of nicotine would account for the illness of the novice as a result of smoking. It would require a high tolerance on the part of the subject to escape disagreeable symptoms with this dose.

UROLOGY.

Pyonephrosis.

IRVING SIMONS (*The Journal of Urology*, April, 1923) considers the factors in the causation of pyonephrosis and the progressive pathological changes involved in this condition. Light has been shed on some of the early ætiological factors by the use of pyelography. It is suggestive that in the condition known as acute septic infarcation of the kidney the distribution of the infarcted areas corresponds to that of the cavities of the typical pyonephrosis. This acute disease of the kidney results from a virulent hæmatogenous infection. A more common forerunner of pyonephrosis is a *Bacillus coli* pyelo-nephritis. The latter when complicated by the presence of kinks, twists or strictures of the ureter of congenital of inflammatory origin is likely to develope by renal destruction into a true pyonephrosis. Obstruction in the pelvis or ureter by calculus is a common cause of pyonephrosis. In an entirely different category lie the conditions causing ascending infection. In short, this variety of infection follows cystitis resulting from stricture, enlargement of the prostate or other bladder neck obstruction, vesical neoplasm or calculus and finally disease or injury of the spinal cord. The renal changes are usually unilateral in the hæmatogenous group and bilateral in the ascending infection group. It is important to observe that in many instances localizing pain may only be slight and the renal destruction may have advanced greatly before severe pain in the side, fever and rigors bring the patient to the medical attendant. Occasional fever and chills may lead the practitioner to a diagnosis of malaria or phthisis. The pyuria is very often of a high degree. If the settled deposit reaches to one-fourth of the total height of the specimen of urine, pyonephrosis may almost certainly be diagnosed, the only other possibility being a vesical diverticulum.

Renal Hæmaturia.

GRANVILLE MACGOWAN (*The Journal of Urology*, April, 1923) discusses renal hæmaturia due to vascular changes in the papillæ of the kidney and reports a recent case. The advent of the hæmaturia is usually without any traceable cause. It is sometimes abundant, frequently intermittent. Pain is rare, but should it be present it is due to obstruction of the ureter by a clot. Diagnosis is made by exclusion using clinical, microscopical, cystoscopic and pyelographic methods in the examination. The investigator should determine the absence of tuberculosis, stone, neoplasm, colon bacillus infection, acute or chronic nephritis, mineral poisoning, scurvy and purpura. The pyelogram should appear normal and the renal efficiency be good. The condition has been found to be due either to dilatation of the venules at the tips of one of the papillæ or to angioma of the papillæ. Splitting open of the kidney with resection of the affected area has been advised, but the writer considers this dangerous from the special risk of secondary hæmorrhage which seems to be associated with this condition. Should simpler means such as intrapelvic injections of a 5% solution of silver nitrate fail, the surgeon should have recourse to nephrectomy.

Perivesical and Pelvic Cellulitis.

F. LEGUEU AND P. ROCHET (*Journal d'Urologie Médicale et Chirurgicale*, January, 1923) discuss the causes and the treatment of the various forms of cellulitis which may occur in the pelvis after cystotomy, suprapubic prostatectomy and partial resection of the bladder. Infiltration of urine from the incised bladder, or suppuration starting from a focus in the prostate, bladder or deep portion of the urethra is the original cause. In order to clear up the trouble open drainage must be provided and must lead down to the *fons et origo*. The suprapubic wound is usually laid open, but in addition the surgeon may have to supply counter drainage in the perineum. In order to drain the suppurating pelvic cellular tissues from the latter aspect the following technique is advised. An incision five centimetres long is made in the perineum a little medial to the pubic arch on the side of the suppuration. The incision is placed over the triangle between the *crus penis* and the bulb; this triangle is then opened up. A large grooved sound is passed through the suprapubic wound down behind the pubis and made to project in the region of the perineal dissection. What remains of the perineal diaphragm is incised on to the sound and a probe is passed along the groove on the sound. The sound is removed and a rubber tube attached to the eye of the probe is drawn into the perineum. The operation may be performed on each side if necessary. Such drainage will be satisfactory even where the suppuration has eroded the pubis, or spread all around the lower part of the bladder. Should the cellulitis have extended, however, to the inguinal canal or into the deep part of the thigh through the obturator canal, further incisions must be made in appropriate situations.

Radium in Cancer of the Prostate.

H. C. BUMPUS (*Radium*, October, 1922) analyses a series of two hundred and seventeen instances of carcinoma of the prostate treated by means of radium at the Mayo Clinic during the last seven years. The chief conclusion reached from this extensive study is that the best results are to be expected from a combination of central (embedding) and peripheral (rectal and urethral applicators) application of the element. One-third of all patients with cancer of the prostate are found at the first examination to have metastases, especially in the pelvic girdle and lower portion of the spine; in only a few instances are the metastases in lymph glands alone. Where the renal efficiency is greatly reduced and the general condition poor, radium treatment is inadvisable. As a rule, more than one-half of the patients are not in a condition to be benefited by radium treatment. The conclusions are drawn from a comparison of the two hundred and seventeen patients treated by radium with two hundred and forty-one patients not so treated. The only definite conclusion is that prolongation of life for about a year occurs in approximately one-fourth of the patients treated with radium.

Radium in Bladder Carcinoma.

G. G. SMITH (*The Journal of Urology*, March, 1923) records his experiences to date with the implantation of tubes of radium emanation or the bromide salt into different varieties of carcinoma of the urinary bladder. Two classes of growth are suitable for this treatment, small, single papillary carcinomata and sessile carcinomata of less than three centimetres diameter which are not so situated as to be readily removed by partial resection of the bladder. In the former condition small glass "seeds" of radium emanation may be implanted through the cystoscope, in the latter it is better to open the bladder and embed needles containing radium bromide. Needles containing radium bromide corresponding to five milligrammes of radium element should be implanted about one centimetre apart and particularly all round the periphery of the growth. Sloughing and infection of the growth area follow in slow course and it is advisable to retain the suprapubic drain for some months in bady infected bladders. The needles of radium bromide should be allowed to remain embedded for twenty-four hours.

Vesico-Vaginal Fistula

H. MCCLURE YOUNG (*Urological and Cutaneous Review*, June, 1923) limits the vaginal approach for repair of vesico-vaginal fistulæ to simple small fistulæ some distance removed from the ureteral orifices. When the fistula is large and involves the trigone and especially if it is near a ureteral orifice the suprapubic transvesical route is preferable. Instruments of great value in the latter operation are a probe, bladder retractor, a knife curved on the flat and a needle-holder of the "boomerang" type as designed by Young. After operation the patient should lie on the abdomen with a retention catheter *in situ* for ten days. Cystoscopic study is helped by packing the vagina with vaseline-smeared gauze to occlude the orifice of the fistula. Similar packing of the vagina before operation lifts the vesical floor so that it is more accessible to the surgeon. The mucosa of the bladder together with the muscle of the bladder wall is dissected up from the vaginal mucosa and these layers are sewn separately together. The bladder is closed completely and drained by means of a de Pezzer catheter retained in the urethra.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Alfred Hospital on August 1, 1923, DR. J. W. DUNBAR HOOPER, the VICE-PRESIDENT in the chair.

Skull Deficiency.

MR. R. C. BROWN demonstrated the post-operative treatment condition of a soldier who had been wounded on October 11, 1917. In November, 1918, there had still existed a gap in the skull of 6.5 centimetres in diameter. The deficiency had been in the site of the left frontal eminence and embraced part of the supra-orbital ridge. The operation of repair by the insertion of split rib grafts had been carried out in November, 1918, and the solidity of the skull in the area of the former deficiency was notable.

Mr. Brown mentioned that an English criticism of the operation was that when cartilage bone was grafted to membrane, bone would be absorbed, so that the ultimate repair would be one of scar tissue. He pointed out the symmetry of the curved sides of the frontal bone and of the supra-orbital ridge, a result which was not obtained by rigid grafts such as those occupied by the tibia.

Mr. Brown exhibited a skull in which was seen a deficiency in the calvarium with the rib sections in positions. He also demonstrated the special chisel used in the operation.

Excision of Urethral Stricture.

Mr. Brown's second patient was a man, aged fifty-two years, who had been the subject of urethral stricture for twenty years. He had been admitted to the Alfred Hospital on March 26, 1923, on account of acute retention of urine. At that time the urethra at the site of the stricture had been quite impervious to bougies. Operation consisted of the excision of 3.5 centimetre of urethra after the method of Mr. Hamilton Russell. At the time of the meeting a No. 14 sound could be passed with ease.

Scrotal Hernia.

The patient, aged sixty-six years, was a wheelwright by occupation and had been under the disability occasioned by a large hernia for fifteen years. He had been admitted to hospital on April 11, 1923, the scrotum being noted at the time as being "as large as a football." Mr. Brown had operated on April 13 and had found that the contents of the hernia included the greater part of the small intestine together with the whole of the omentum and transverse colon. The latter structures were bound together by extensive adhesions which also attached them to the greatly thickened enveloping tissues. The testis was observed to be very large. A filigree was inserted so that the inner end lay behind the conjoined tendon and the operation was completed by the Bassini method.

Mr. Brown exhibited a filigree of the type employed in this instance and a photograph of the enormous hernia as it had existed before operation.

Gastric Carcinoma.

Mr. Brown's fourth patient was a man, aged forty-eight years, upon whom he had performed the operation of partial gastrectomy for the removal of a carcinoma of the stomach.

The duration of symptoms was nine months. During this period the patient had been unable to eat solid food, especially meat, because of the pain it provoked; he had sustained life on milk foods and had lost sixteen kilograms in weight. Though he rarely vomited, he had been occasioned much distress by frequent eructations of a putrid odour. He had been a subject of gout of twenty years' standing and for eighteen months had experienced recurring attacks of anginal pain.

On physical examination a tender epigastric tumour had been palpable; the pulse tension had been found to be 200 millimetres of mercury and the general nutrition had been very poor.

Operation had been undertaken on April 23, 1921, by the anterior Pólya method. The growth had occupied the pyloric portion of the stomach and its extension along the lesser curvature had necessitated the removal of two-thirds of the organ. Dr. Trinca had verified miscroscopically the clinical diagnosis of carcinoma.

Within fourteen days the patient had been hungry and had insisted on eating ordinary meals. He had rapidly gained in weight and had returned to his work, which was that of foreman in a motor garage, one month after the operation. He had worked continuously since. His weight at the time of the meeting was seventy-seven kilograms (twelve stone, three pounds) as against 57.2 kilograms (nine stone) at the time of operation. He still experienced occasional attacks of flatulent discomfort and at intervals was troubled with anginal pains.

Mr. Brown showed another patient whose operation for gastric carcinoma, confirmed microscopically, had been performed twenty-one months previously. In this instance also the Pólya method had been employed, but the tumour had been adherent to the liver and pancreas. The condition of the patient could be estimated from the facts that he was 79.5 kilograms (twelve and a half stone) in weight, that he felt strong, enjoyed his food, in respect to which he was under no restrictions and was able to follow his vocation of a plumber.

Mr. Brown commented on the unexpectedly good state of the patient in consideration of the fact that his age at the time of the operation was only forty years.

A specimen of a gastric carcinoma was also exhibited. It had been resected on July 14, 1923, and had occupied the middle third of the greater curvature of the stomach being adherent to the pancreas and transverse colon. A microscopical diagnosis of carcinoma had been supplied by Dr. Trinca.

In this instance the patient, a female, had exhibited rapid wasting and anæmia which she stated had been present for three months. She had suffered much from a sore tongue and mouth, but had experienced no nausea, no vomiting, no hæmatemesis, no epigastric pain after meals.

She had been observed to have a well defined leukoplakia of the tongue and buccal mucous membrane and a large, elongated, immobile tumour had been apparent in the epigastrium.

Operation had been undertaken by the anterior Pólya method. In connexion with the specimen displayed, Mr. Brown commented on (i.) the contrast between the extent of actual disease and the paucity of symptoms, (ii.) the rapid recovery of appetite and digestive capacity after excision of the tumour, (iii.) the rapid amelioration of the state of the mouth, (iv.) the operability of the large stomach cancer.

Chronic Gastric Ulcer.

Mr. Brown further showed a man, aged fifty-four years, who for five years had suffered from præcordial pain, flatulence, nausea and vomiting. Pain had been aggravated by the ingestion of food; there had been no hæmatemesis. During the five months preceding operation the patient had lost in weight and strength very rapidly and had suffered severe pain, the only relief for which was voluntary emesis.

Operation had been performed by the Pólya technique on June 23, 1923, and had disclosed a very thick-walled ulcer straddling the lesser curvature. Dr. Trinca's report on the microscopical section was that it was one of simple as distinct from carcinomatous ulcer.

The patient had returned to work in seven weeks and had continued at his occupation of joiner ever since. His weight had been increased by thirteen kilograms.

MR. HAMILTON RUSSELL demonstrated the methods he was using in the treatment of fractures of the upper extremity. No splints were employed, the entire armamentarium consisting of a supply of plaster of Paris, crinoline bandages, wool, lint and ordinary bandages.

All injuries of the upper arm from fracture of the clavicle to fracture of the shaft of the humerus included were treated in the same way, *id est* by means of a simple system of bandaging the arm to the side with the forearm slung at right angles across the chest. Over all a few turns of plaster of Paris bandage were run, not for rigidity, but for tidiness and security.

All fractures of the forearm, wrist and fingers were treated by the fitting of plaster of Paris moulds to the broken part. The mould consisted of a piece of lint cut of liberal size to fit over the fracture; upon this laid on a table was prepared a covering of plaster of Paris by means of successive turns, backwards and forwards, of plaster bandages. The mould was laid on the limb, lightly bandaged on and the mould and the fracture were held together in good position while the mould was setting.

Mr. Russell showed a little girl who had been under treatment for three weeks for very bad fracture-dislocation of the elbow. He preferred to treat such injuries by means of a thick mass of cotton wool securely bandaged so as to envelop the elbow; the arm was slung at a right angle under the clothes. He considered this plan safer and better than the full flexion method.

He was particularly emphatic in denouncing the use of passive movement in the after treatment of fractures involving joints, more especially the wrist and elbow joints. A man was shown who had been released on the previous day; he had sustained a fracture of the trapezium and the affected part had been completely immobilized for eight weeks.

Mr. Russell looked forward to the time when the general practitioner would not think it necessary to supply himself with an assortment of splints, but would be able to rely instead on a tin of plaster bandages.

Teratoma of Right Pleural Cavity.

MR. J. S. BUCHANAN presented a female patient, aged twenty-two, who had first sought treatment two years previously on account of the recurrences of swelling in the tissues of the lower part of the neck. She had also had a severe cough and had had occasional slight hæmoptysis. Her weight had diminished from sixty-five kilograms to thirty-six kilograms. By examination with the fluorescent screen a rounded, dense shadow had been observed in the right side of the thorax, bounded below by the diaphragm and on the left side by the heart. It had been considered that the shadow was probably thrown by an hydatid cyst.

In April, 1920, the thorax had been opened by the removal of several rib cartilages and portion of the sternum and a large amount of sebaceous débris and hair had been evacuated from the cyst. In August, 1920, a pedunculated mass had been removed by *écraseur*. A similar mass had been removed three weeks later. The cavity was being permanently drained by means of a silver tube and the patient was in good general health, her weight being sixty-five kilograms.

Dislocation of the Knee.

Mr. Buchanan's second patient, a man, aged twenty-six years, had sustained a lateral dislocation of the right knee in September, 1920, when his lower limb had been caught in the belting of some machinery. It had been noted that there was no bone injury. After reduction of the dislocation immobilization of the joint had been secured by the application of a posterior splint with foot-piece attached. Subsequently the limb had been encased in plaster of Paris, after which the patient, having been in hospital twelve days, had been discharged. The plaster had been reapplied two months later and after the lapse of a further eight weeks had been replaced by a "gutter" splint behind the knee.

The patient had not been allowed to place any weight on the injured knee for a period of five months; six months after the injury he had returned to work having been fitted with a "Marsh" splint to prevent over-extension. He frequently went about without artificial support.

Excision of the Rectum.

Mr. Buchanan showed a woman, aged fifty-two years, who had been admitted to the Alfred Hospital in April, 1922. The diagnosis of malignant disease of the rectum had been established. Operation had been performed in two stages. The first consisted of exploratory laparotomy and left inguinal colostomy, and the second two weeks later comprised excision of all the bowel below the colostomy by the combined abdomino-sacral route. It was twelve months since the patient had been discharged from hospital.

Multiple Gummata.

MR. JOHN KENNEDY discussed the case of a girl, aged twelve years, affected with gummatous disease of the left femur. Symptoms had begun two years previously and the pathological process had progressed to abscess formation; this had led to incision and subsequent secondary infection.

The girl had first come to the Alfred Hospital four months previously; prior to an operation for the removal of sequestra a skiagram had been taken. It had disclosed destruction of the head of the femur and acetabulum with new bone formation round the neck of the femur. Improvement was shown in a very recent skiagram and in the condition of the limb.

A swelling which had been present under the extensor tendons of the left wrist when the child had first come to hospital, had been regarded as of tuberculous nature and this view had been supported by the radiographic appearances and by the cutaneous reaction to bovine tuberculin. Operation had revealed that the disease process was more probably gummatous and several small sequestra had been removed from the distal extemity of the left ulna. Skiagrams were exhibited for comparison of the state of the bone at the time of the girl's admission with its condition at the time of the meeting. A reaction had been reported when the blood was sent for investigation by the Wassermann test.

Mr. Kennedy intimated that his object in showing this patient was to illustrate the clinical simulation of a tuberculous by a syphilitic process.

Multiple Renal Calculi.

A woman who had been operated upon at the Lady Curzon Hospital, Bangalore, was in possession of five calculi, two of which were very large, that had been removed from her right kidney. Nephro-lithotomy had been performed seven months prior to her appearance at the Alfred Hospital two months previously, when it had been found that a sinus had persisted in the operation area and by X-ray examination that a small calculus was embedded in the right kidney. This stone had been giving rise to no symptoms.

Mr. Kennedy had catheterized the ureters and had found that on the right side there had been a delay of only three minutes in the appearance of indigo-carmine; the urine had apparently been normal and had been free from pus and bacteria. It was interesting to note that a kidney so severely damaged had retained such a good degree of functional efficiency.

Pott's Fracture.

Mr. Kennedy's third patient was a man who had sustained a Pott's fracture, accompanied by dislocation of the astragalus twelve months previously. When he had presented himself at the Alfred Hospital six months later he had sought correction of the mal-union as a result of which his foot had been fixed in a position of extreme internal rotation. Osteotomy of both malleoli had been performed, the dislocation had been reduced and the foot had been fixed in such a manner that the deformity had been over-corrected. There had been a slight degree of recurrence of the general displacemnt, but the man had returned to work. He had been fitted with an inside iron with "T" strap on the outer aspect of the leg and wore a boot which was blocked up on the inner side. Two skiagrams were exhibited illustrative of the deformed and corrected positions of the foot.

As illustrating the routine treatment of Pott's fracture, Mr. Kennedy showed a man who had met with this acci-

dent six weeks previously. The deformity had been reduced under anæsthesia and the correct position had been maintained by means of a double plaster "gutter." The patient was walking about, wearing a boot which was blocked up on the inner side.

Multiple Fractures.

MR. BALCOMBE QUICK demonstrated skiagrams relating to a patient who had sustained fractures of the right femur and patella, a Y-shaped fracture of the lower end of the left femur, fractures of the olecranon process on the left side and of both internal cuneiform bones. The accident which had resulted in this schedule of injuries, was a fall from a height of six metres (twenty feet).

The right femur had been treated by a plating operation and at a later period, arthro-plasty had been performed for the relief of the patello-femoral ankylosis. The injury to the left femur had been repaired by nailing the condyles.

Bone Grafting.

In the second instance Mr. Quick had operated for the repair of a deficiency in the tibia consequent on a gun shot wound leading to a compound fracture of both bones of the leg. He had employed bone grafts, an intramedullary splint, ten centimetres in length, of the opposite fibula in its whole circumference and a sliding inlay graft taken from the opposite tibia. The wound throughout its extent had become acutely inflamed and suppuration had ensued, so that it had become necessary to remove the grafts. The inlay graft had been removed twelve weeks and the intra-medullary graft twenty weeks after the original operation.

A series of radiograms illustrated progressive bone formation at the site of the inlay graft in spite of the septic infection and total absence of bone formation from the intra-medullary splint. They were shown to demonstrate the superiority in bone formative powers of those grafts in which cancellous structure and marrow are freely exposed.

Dislocation of Knee Joint.

Mr. Quick showed a man in whom dislocation of the knee joint had occurred twelve months before. The joint had been completely immobilized for seven months in a plaster cast and the patient had a completely stable and painless joint in which there was only slight lateral mobility. Flexion was limited to an agle of 30°, but the range of movement in this respect was steadily increasing.

Recurring Dislocation of Shoulder Joint.

Dislocation of the shoulder joint had occurred five times in the course of twelve months in a man whom Mr. Quick had treated by the operation of reefing of the lower portion of the capsule of the joint. Seven months had elapsed since the operation and there had been no dislocation since, although the man was in active work as a gardener.

Arthrotomy of Knee Joint.

In another patient Mr. Quick had gained access to the knee joint for the removal of a loose internal semilunar cartilage by vertical splitting of the patella. He commented on the rapid convalescence and perfect functional result which had followed the operation.

A Case for Diagnosis.

Mr. Quick presented a boy, aged ten years, for suggestions in regard to diagnosis. He had been admitted to the Alfred Hospital on January 12, 1923, suffering from acute osteomyelitis of the upper end of the left humerus of five days' duration. Subsequently numerous metastatic abscesses had developed, included among which were foci of suppuration in the left elbow joint and in the left radius. On March 16, 1923, high amputation of the left arm had been performed. Early in April œdema of the right arm, right side of the chest and abdominal wall had appeared, accompanied by evidence of fluid in both pleural cavities, particularly the right, and ascitic effusion. The liver had become enlarged, extending to the umbilicus and very tender. A little later the right external jugular vein had become visibly distended even on deep inspiration; the face had been observed to be full and puffy and the lips cyanosed.

The right pleural cavity had been aspirated on three occasions; twice slightly turbid fluid had been withdrawn and more recently clear fluid. Clear fluid (one hundred and fifty cubic centimetres) had been withdrawn from the left side of the chest on July 30, 1923. The temperature had been gradually declining, but still showed rises to 38° C. or 39° C. at intervals. The boy's general condition was good and he ate and slept well.

The œdema had apparently diminished during the last few weeks and the ascitic collection was less; the liver still extended to the umbilicus, but was less tumid and was not tender. It had been noted that a collateral circulation was developing between the external jugular and intercostal veins. X-ray examination had failed to demonstrate any mediastinal shadow.

MR. FAY MACLURE demonstrated from a number of patients.

Pitchfork Injury to the Base of Brain.

A man, aged twenty, while working on a haystack in November, 1922, had slipped and a pitchfork prong had penetrated the left nostril. Injury to the base of the brain had resulted affecting the left optic nerve and optic tract and probably the left *crus cerebri*. He exhibited a right-sided hemiparesis which was tending to recover and a partial degree of anæsthesia on the right side. The tendon reflexes were exaggerated on the right side and on this side also the plantar reflex was extensor in character. The left pupil was seen to be larger than the right and it was inactive to direct light. The eye movements were good in all directions with the exception that the left eye failed in convergence; there was no perception of light in the left eye and ophthalmoscopic examination disclosed primary optic atrophy on this side. The field of vision in the right eye had been determined and the chart was exhibited to show the temporal hemianopsia.

Tuberculoma of the First Rib.

A provisional diagnosis of tuberculoma of the first rib had been made in the case of a man, aged twenty-nine years, whose history of symptoms dated back to 1915. He had then been discharged from the military forces as medically unfit and had suffered much pain from "rheumatism" in the right shoulder.

In 1918 he had undergone the operation of left orchi-epididymectomy for tuberculous disease of the left epididymis and after the operation had exhibited wrist-drop, which had disappeared six months later. During 1920 and 1923 the patient had exhibited every June attacks of weakness in the muscles of the left arm. His blood serum had not fixed complement in the tests for syphilis and hydatid. The von Pirquet cutaneous tuberculin test resulted in a strong reaction to human tuberculin. Skiagrams were exhibited from which it appeared that there was a pathological process in the first rib.

Injury to Foot.

Mr. Maclure presented a girl, aged eight years, who on February 27, 1923, had fallen a distance of two metres (seven feet) in such a manner that her left foot had doubled under her. A radiogram revealed fracture of the four medial metatarsal bones; that of the great toe was fractured near its base and its shaft was displaced in a downward and outward direction. As wrenching had failed to replace the bone, a hook had been passed round it in order to exert direct pull. At the time of the meeting the foot had been in plaster of Paris for five weeks.

A second instance of injury to the foot was shown for the purpose of eliciting opinions regarding the diagnosis. The patient, a youth of sixteen years, had suffered pain in the left foot for the past eighteen months, the onset having followed a slight injury. Three years before the date of the meeting both little toes had become swollen and inflamed. Radiograms were exhibited and it was stated that the blood serum failed to react to the Wassermann test.

Ulnar Paresis.

M.W., aged thirty years, had exhibited symptoms of ulnar pressure and paresis for the past six years; the disability was of a progressive character and had supervened on an old fracture of the elbow which dated back twenty-two years. Mr. R. C. Brown had operated eight weeks previously for the sub-periostal reformation of the ulnar groove in the humerus. Some improvement had been shown to date.

Cervical Ribs.

MR. A. J. TRINCA exhibited some skiagrams of the chest of a female patient, aged forty-one years. For the last six months she had complained of pain and swelling in both wrists and stated that these features were aggravated in the mornings on rising. At times the veins on the dorsum of the hands became distended. On physical examination no anæsthesia could be detected and there were no objective signs to be observed in the wrist joints. The skiagram disclosed bilateral enlargement of the transverse processes of the seventh cervical vertebra.

Lesion of Brachial Plexus.

Mr. Trinca's second patient was a miner, aged thirty years. On August 24, 1922, a tree had fallen on his right shoulder and leg as a result of which accident he had spent sixteen weeks in a country hospital. When he left that institution his right arm had been almost powerless.

He had first attended the Alfred Hospital on December 22, 1922, when the injured arm had been observed to lie passively by his side, while the hand was supported by his left hand. Muscular wasting, especially in the deltoid, had been advanced and the only movement of which the arm was capable, had been slight flexion at the elbow when the forearm was pronated.

Mr. Trinca supplied a table of the electrical reactions of the muscles of the arm and forearm.

Operation had been undertaken on January 12, 1923, when the nerve trunks had been exposed below the clavicle and a large amount of perineural scar tissue had been removed. The outer and posterior cords of the brachial plexus had been found to be softened and unresponsive to stimuli. Since operation there had been constant improvement in all the muscular movements except those controlled by the fifth cervical segment. The arm had been kept in an abduction external rotation frame; frequent electrical stimulation had been applied and active educational movement instituted.

Sarcoma of Maxilla.

MR. H. BARRY THOMSON presented a man, aged thirty years, for whom he had performed excision of the maxilla for sarcoma of the left maxillary antrum three years previously. For a time the patient had suffered from diplopia, but this had ceased to trouble him. The palatal deformity was filled in with a hollow box denture made by Mr. Kenneth Russell. The denture in position conferred a natural appearance to the face and normal quality in the voice. Since the operation the man had gained 13.5 kilograms in weight. The operative incision was scarcely visible and the deformity hardly noticeable.

Frontal Sinusitis.

A man, aged twenty-seven years, affected with chronic frontal sinusitis, had been a difficult subject for operative treatment on account of the presence of a very large nævus in the right frontal region. An almost vertical incision had been made in order to avoid the nævus which had been held aside while the whole anterior wall of the sinus had been removed. The sinus was of the large, shallow type and although no nasal bridge was left, there was very little ultimate deformity.

Chronic Otitis Media.

Mr. Barry Thomson showed a woman, twenty-five years of age, who had been affected with bilateral *otitis media* for twenty years. Five years previously the radical mastoid operation had been performed on the right side, but on the left side the more conservative operation had been adopted, the ossicles and the remains of the tympanic membrane being preserved. Her hearing was on the whole very good, being almost normal on the right side, the site of the radical operation and not quite so good on the side of the more conservative operation. Meatal flaps had been utilized on both sides.

Another woman had been affected with *otitis media* on the left side for twenty-five years. Altogether six mastoid operations had been performed, the last having been a radical operation two and a half years previously. On that occasion large masses of cholesteatoma had been removed. The ear was quite dry, but the hearing on the side was not good and in this respect she had not done as well as the former patient.

Intra-Nasal Tumour.

Mr. Barry Thomson showed a female patient, aged fifty-one years. She presented a swelling, visible and palpable in the floor of the nose and extending into the right canine fossa. The swelling was of twelve months' duration and was quite painless. By the radiogram the right maxillary antrum was seen to be quite opaque. There was a history of a fall from a motor car three years before, involving injury to the right side of the face. The swelling was of cystic character as estimated by palpation and it appeared to be either a new growth or a developmental residue.

Acute Mastoiditis.

DR. BRYAN FOSTER detailed the case of a man, aged sixty years, who when first seen three weeks before, had given as history that five months previously he had been seized with sudden earache; this had been followed within a few days by discharge and otorrhœa, accompanied by more or less pain had continued ever since. Examination had disclosed free purulent discharge from the middle ear through the meatus, sagging of the posterior meatal wall and deep mastoid tenderness. The patient had looked ill; his pulse-rate had been 120 and his temperature 38.8° C..

Immediate operation had been performed, but had been limited to opening and curetting the mastoid antrum and several large cells, interference with the middle ear and the meatal wall having been avoided. After-treatment had been confined to changing the gauze drain in the post-auricular wound. Within twelve days the middle ear had healed and hearing had recovered to 80% efficiency.

Dr. Foster's object in showing this patient was to illustrate the fact that suppurative *otitis* of long duration would frequently clear up promptly if direct drainage through the mastoid process were provided. As compared with the Heath operation the procedure involved much less trouble to both patient and surgeon.

Pituitary Tumour.

DR. E. L. GAULT demonstrated that a patient suffering from the effects of a pituitary tumour, had optic atrophy in one eye and normal vision in the other.

He also showed as a possible instance of von Mikulicz's disease a patient in whom were evident bilateral tumours of the submaxillary gland.

A number of patients were shown for ophthalmoscopic examination of various forms of retinitis and chorioiditis. Glioma of the retina was exemplified in an infant.

Chorioidal Tubercles.

DR. J. RINGLAND ANDERSON exhibited a specimen of an eye in which chorioidal tubercles and swollen optic disc could be readily discerned with the aid of a hand lens.

Rheumatoid Arthritis.

DR. HENRY LAURIE showed a number of patients affected with rheumatoid arthritis whom he had treated by intravenous injection of *Bacillus coli* vaccine as detailed in his paper in THE MEDICAL JOURNAL OF AUSTRALIA of March 24, 1923 (page 309).

Nephritis.

DR. WALTER SUMMONS presented a number of patients, subjects of nephritis of various clinical types and discussed the urea concentration test and blood urea estimation with

reference to the assistance derived from them in classifying the clinical varieties of nephritis and in arriving at a prognosis. He held that the tests were nearly always consistent with the clinical course of the disease.

The disease in the first patient, a male, aged thirty-four, he regarded as of mixed hydræmic and azotæmic type. The man had suffered a uræmic convulsion on the night prior to the meeting and it was to be noted that his blood urea had been determined as 81.5 milligrammes per hundred cubic centimetres of blood.

The urine was of specific gravity below 1010, and contained albumin and casts. Greatly impaired renal efficiency was indicated by the urea concentration test, in which the amount of urea in the urine passed at the end of the second hour after the ingestion of urea was only 1.7%.

In the case of a female patient, aged forty-two years, who displayed general anasarca, orthopnœa with circulatory failure, blood pressure of 160 millimetres of mercury, albuminuria and urinary casts, the blood urea was 19.7 milligrammes per hundred cubic centimetres. Estimations of the urea content of the urine passed at the end of the first and second hours after the ingestion of urea gave readings of 0.7% and 0.9% respectively. Kidney function was evidently very poor, but it was difficult to explain the low figure for blood urea.

A male, aged thirty-one years, had been admitted to hospital in an hydræmic state. Œdema had disappeared after one week's regulation of the diet which had been rendered salt free and had consisted largely of milk and water. The systolic blood pressure had registered 140 millimetres of mercury. Estimation of the blood urea and the urea concentration test had been carried out subsequent to the disappearance of the œdema. The urea had been 52.5 milligrammes per hundred cubic centimetres of blood and the amount of urea passed during the second hour was 1.2%. It would appear that in this patient an acute exacerbation had supervened on a chronic interstitial nephritis, or the nephritis, acute in nature at the onset, had been followed by interstitial changes. The only possible ætiological factor that could be determined, was a febrile illness of fourteen days' duration and accompanied by cough, six weeks prior to the onset of the œdema.

In contrast with the three preceding were two other examples in which the prognosis was good.

A woman, aged thirty-five years, dated her ill-health from child-birth four years previously. Symptoms of infection of the urinary passages had been very troublesome for three years and for a long time she had displayed general anasarca, with associated albumin and casts in the urine. She was at the time in good health and free from symptoms. Urea concentration tests had been carried out on May 9 and on July 18, 1923, and on both occasions the percentage of urea in the urine of the second hour had reached 2.5%. The blood urea had been determined to be thirty-one milligrammes per hundred cubic centimetres on July 18, 1923.

An old man, eighty-three years of age, had been an in-patient of the hospital on account of cardiac failure and general œdema. His systolic blood pressure had been 170 millimetres of mercury. The urea concentration test had been carried out on April 18, 1923. Before the ingestion of urea the amount of urea in the urine had been 1.6%. In that of the first hour after the urea meal, it had been 1.35%, and in that of the second hour it had risen to 2.9%. A determination of the blood urea had been carried out on July 11, 1923, the reading having been forty-four milligrammes per hundred cubic centimetres of blood.

Dr. Summons considered the condition of this patient as an example of arterio-sclerosis rather than nephritis.

Paroxysmal Tachycardia.

DR. M. D. SILBERBERG showed a male patient who was subject to frequent attacks of paroxysmal tachycardia which were very well depicted in the polygraph tracings displayed.

In two other patients auricular fibrillation had been steadied to a regular heart beat by the exhibition of quinidine sulphate.

Radiographic Diagnosis of Pulmonary Tuberculosis.

DR. W. S. NEWTON showed a series of thoracic skiagrams of individuals affected with pulmonary tuberculosis; all had had hæmoptysis and the X-ray photographs had demonstrated definite lesions before physical signs could be detected. The skiagrams were kindly lent by Dr. K. Stuart Cross.

J.K., aged twenty-four years, an ex-soldier, had been taken ill with pleurisy in France in 1918. His recent history embraced loss of energy and irritating dry cough for four weeks. Two days before examination he had expectorated a small quantity of blood. The only physical sign elicited had been a slight rise in pitch over a limited area at the apex of the right lung. The radiologist's report was that there existed an area of increased density in the right apical area. One month later tubercle bacilli had been demonstrated in the sputum.

A second radiogram of this patient's chest, taken after seven months' treatment, showed considerable diminution in the area affected.

C.J., aged thirty-two years, an ex-soldier, had contracted influenza with pneumonia in France in 1918. He had sought advice on account of loss of energy for three months and by reason of the fact that on the day prior to examamination he had coughed about ninety cubic centimetres of blood. No abnormal signs had been evident to physical examination. A skiagram revealed an area of increased density at the right hilus and mottling at both apices. Six weeks later occasional post-tussive crepitations had been heard over the apex of the right lung and tubercle bacilli had been found in the sputum. Three weeks before his first examination this patient had been accepted as a "first class life."

Mrs. L.N., aged twenty-three years, whilst playing tennis had suddenly coughed a considerable quantity of blood. She had been examined on the same day, but no physical signs had been detected.

By X-ray examination it had been shown that there was some increased density in the hilus of the right lung accompanied by "mottling" of the apical area on the same side. At the end of one month the patient had felt well and had demurred at further treatment. Three months later she had reported again and on this occasion prolonged expiration and post-tussive crepitations had been found in the right inter-scapular space. Tubercle bacilli had then been found in the sputum.

R.Y., an ex-soldier, aged twenty-three, had had influenza with pulmonary complications and in 1921 had been admitted to No. 11 Australian General Hospital with pleurisy. Some time after his discharge as fit, he had become troubled with a slight morning cough and increasing lassitude. A small hæmoptysis had occurred two days prior to physical examination which had revealed occasional crepitations in the right inter-scapular space. These had disappeared and had not been heard at subsequent examinations carried out during the next three weeks.

The skiagram disclosed an area of abnormal density behind the sternal end of ths first intercostal space on the right side. Six weeks later a small specimen of sputum had been obtained and tubercle bacilli in small numbers had been demonstrable.

J.M., aged twenty-six years, had sought advice on account of cough, loss of weight and increasing lassitude. Although he had been examined by four physicians independently, no physical signs of an abnormal character had been found.

By the skiagrams there was seen to be present an extensive hilus lesion on the right side. Tubercle bacilli had been found in the sputum.

In this instance it was seen how extensive a lesion spreading from the hilus might become before physical signs could be determined.

A female patient, aged thirty-two years, was affected with an advanced lesion at the apex of the right lung, readily demonstrated by both physical and radiological examination. At the time of the first examination she had

lost over a half of a litre of blood in eight hours by repeated hæmoptyses. As the condition was unilateral, the right lung had been compressed with excellent results.

Dr. Newton exhibited and demonstrated the method of employing the nitrogen compression apparatus by the induction of artificial pneumothorax.

Spondylitis.

DR. C. E. DENNIS displayed a series of radiograms in each of which was disclosed more or less degree of spondylitis. The point of interest about these plates was that they were obtained from patients who had been referred for X-ray examination on account of pain which was suspected to be due to renal or biliary colic.

Two other photographs exemplified the X-ray findings after the ingestion of barium in the presence of duodenal ulcer.

A MEETING OF THE WESTERN AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Perth Hospital on July 18, 1923, DR. D. M. MCWHAE, C.M.G., C.B.E., the PRESIDENT, in the chair.

Parkinson's Disease.

DR. D. M. MCWHAE presented a man, aged twenty-seven years, the subject of Parkinson's disease or *paralysis agitans*. He had complained of stiffness of the legs and difficulty in walking, stiffness and trembling of the arms which prevented him from carrying on his work as a compositor, hesitancy and monotony of speech and loss of weight, amounting to nineteen kilograms (three stone) in the course of three years. When examined the patient had presented the physical signs of *paralysis agitans*. His face was mask-like; there were tremor and loss of the finer movements of the arms, chiefly the left, and the characteristic speech and gait. The patient had stated that the trouble had begun two months previously. Dr. McWhae held that this and the evident sleepiness suggested the possibility of an association between *encephalitis lethargica* and the Parkinsonian syndrome. This combination was not rare when the basal ganglia of the brain were effected by the inflammation. A week after admission he had questioned the patient's wife who maintained that the condition had been coming on slowly and insidiously. The loss of energy had first become noticeable over three years before. The mask-like facial expression had appeared over two years previously and the stiffness of the arm twelve months previously. The speech had become involved six months before admission. There had not been any complaint of headache nor had there been vomiting. At the time of admission the deep reflexes had been exaggerated, but there had been no sensory defect. The only history of a past acute illness that had been elicited was that of a feverish attack in Sierra Leone in 1916. This might have been malaria. He had made rapid recovery and had subsequently served for three years in the Australian Imperial Force.

Dr. McWhae had come to the conclusion that the condition was Parkinson's disease which had begun when the patient was only twenty-seven years of age. He had seen another patient in whom this disease had begun at the age of thirty-five, but as a rule *paralysis agitans* was a disease of old age. The disease had been recorded in persons as young as sixteen, fifteen and twelve years.

Lupus Erythematosus.

DR. F. L. GILL showed a patient with *lupus erythematosus*. The patient was a female. She had noticed the condition of the skin in September, 1922. From that time she had been under treatment for nine months without noticeable improvement. Carbon dioxide snow had then been applied over the whole of the affected area. The distribution was the usual one, across the bridge of the nose, involving both malar regions. The result of the treatment had been satisfactory. The patient had been free for seven months. There was very faint scarring.

Tabes Dorsalis.

Dr. McWhae's second patient was a man who had been ill for fourteen years. The illness had begun with staggering and occasional attacks of vomiting. Eight years before admission the right shoulder had been dislocated painlessly and two years later a similar dislocation had been reduced by operation and no recurrence had taken place. Examination revealed the absence of the knee jerks, the presence of Argyll-Robertson pupils and other signs of *tabes dorsalis*. There was an enormous hypertrophic growth of bone at the head of the right femur forming a Charcot joint. A similar overgrowth was present of the left shoulder joint. Dr. McWhae called attention to another interesting feature. It was the presence of gummata. This was not a common occurrence in *tabes dorsalis*. Twelve months previously a gumma had appeared in the left shoulder. It had healed rapidly under treatment with "Salvarsan," mercury inunctions and iodide of potash given internally. Later another gumma had appeared which had not healed at the time of the meeting. He was under treatment for it.

Exophthalmic Goître.

Dr. McWhae showed two men, both affected with exophthalmic goître. The condition had been present for thirteen years in the one and for eight years in the other patient. The characteristic signs were present. Both patients were completely incapacitated from work on account of myocardial degeneration. He had brought these patients to the meeting in order to obtain opinions as to whether anything further could be done for them. Hale White had inquired into the after history of all patients admitted to Guy's Hospital between 1888 and 1907 and of all his private patients during the same period. He had come to the conclusion that the mortality of persons with exophthalmic goître was not much higher than that of the general population. That meant that it was a disease with a natural tendency toward recovery. It was rarely seen in elderly people. He had further concluded that there was not sufficient knowledge to settle the difficult question whether or not an operation should be performed. Dr. McWhae stated that every practitioner recognized that some patients recovered. Rest, the removal of septic foci, exposure to X-rays and the exhibition of suitable drugs occasionally enabled these patients to recover their equilibrium and to become normal. These measures should therefore be given a thorough trial before operation was entertained. T. Dunhill had expressed the opinion that very many patients with exophthalmic goître ultimately reached the state in which the two patients shown had arrived. He had differed from Hale White and maintained that all patients should be operated on if they did not respond to medical treatment. He removed one lobe of the thyreoid gland and, if this did not turn the scale toward recovery, he removed a portion of the other lobe.

One of the patients had been sent to him nearly thirteen years before by T. Dunhill. One lobe of the thyreoid gland had been removed with great benefit to the patient. He had been able to resume his occupation for eight years. He had then broken down and for three years had been unable to work. It appeared that operation in this patient had at the best only delayed the progress of the disease for some years. The result might have been better had a portion of the other lobe been removed. The double operation had been T. Dunhill's practice for many years. Dr. McWhae said that he would be glad of any opinion on the advisability of further treatment for the two patients.

Arthritis of Indefinite Origin.

Dr. McWhae brought forward two patients with arthritis. Both were women. In one the hip joint and in the other the knee joint was affected. Both patients had been carefully examined for the presence of septic foci, but none had been found, other than a few decayed teeth in one of them. The tonsils, the teeth, the urine and the vagina had been examined. Skiagrams had been taken of both and were shown, as was a skiagram of the hip joint of a third patient under his care outside the hospital. In the knee joint there was only a slight bony change, a rarefaction of the outer articular surface and of the external condyle of the femur. In the hip joint of the hospital patient there were only moderately extensive changes in the bone, but in the other there was complete destruc-

tion. In both patients the diagnosis of sciatica had been made. The treatment consisted chiefly in improving the general health by dietetic means and by giving iron and arsenic. The joints were immobilized and one patient received a gonococcal vaccine, as a Neisserian infection was suspected. Massage and passive movements would be employed at a later date.

Intolerance to Iodine.

DR. DAVIES showed a patient who exhibited an iodide rash after the administration of three centigrammes (five grains) of iodide of potash.

Fracture-Dislocation of the Elbow.

MR. F. A. HADLEY presented a patient who had sustained an injury of the right elbow. The trauma had lead to a fracture-dislocation. A skiagram was also exhibited.

Lipoma and Cystic Kidney.

DR. M. K. MOSS showed a patient with a large lipoma in the right flank and cystic kidneys.

Elephantiasis of the Scrotum.

DR. A. JUETT presented a patient who had had elephantiasis of the scrotum. Mr. Hadley had operated on the patient.

Infective Granuloma.

DR. J. KENNY exhibited a patient with infective granuloma. The condition had been treated with antimony tartrate. The Wassermann test had been applied but the serum had not yielded a reaction.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been nominated for election as members of the New South Wales Branch of the British Medical Association:

EDWARDS, ALFRED THEOPHILUS, M.B., 1922 (Univ. Sydney), The Hospital, Callan Park.

FORSYTH, GORDON, M.B., Ch.M., 1922 (Univ. Sydney), Bundock Street, Coogee.

JENKINS, ARCHIBALD, M.B., Ch.M., 1923 (Univ. Sydney), 14, Oxley Street, Glebe Point.

Correspondence.

"INSULIN."

SIR: It is with regret and no small degree of astonishment that we have read the editorial in the issue of September 1 of THE MEDICAL JOURNAL OF AUSTRALIA. We fail to perceive any foundation in fact for the unfavourable opinion of "Insulin" which the writer of the article has formed and we consider that our articles in the preceding issue have been misinterpreted and misrepresented in several particulars.

The writer states that a considerable period will have to elapse before the full therapeutic significance of this preparation can be ascertained. To this statement no one can possibly take exception. But when he goes on to say that: "In the meantime, no doubt, hundreds of diabetics will be hastened to their graves by its means," we can only deplore the fact that a statement so utterly at variance with all the known facts of "Insulin" therapy should have found a place in the editorial columns of the responsible medical journal. "Insulin" has been in therapeutic employment in England, Canada and the United States for over a year and not only are the reports from the most authoritative sources unanimously favourable to its use, but no single case of death attributable to its employment has ever to our knowledge been reported. Only one instance of overdosage has been reported to the Medical Research Council and that was controlled by the simple measure of administering glucose. Exhaustive experiments upon animals and clinical experience concur in showing that "Insulin" only becomes dangerous when the overdosage is so great as to induce a very profound hypoglycæmia and it is already a well-established fact that the mere administration of glucose to correct this hypoglycæmia suffices to arrest or avert untoward symptoms. It is especially regrettable that this alarming and unfounded prediction should have found its way into the columns of the lay press.

The writer goes on to state that our articles do not provide an unequivocal reply to the question of the value of "Insulin" in the treatment of diabetes. This statement is manifestly absurd since our investigations, in common with those conducted elsewhere, show perfectly clearly that "Insulin" is of definite utility as an adjuvant to dietetic treatment and especially as a means of combating the acidosis which is the cause of the ultimate fatal outcome of diabetes. No one has ever suggested that it cures the pathological lesion on which the disease rests nor has anyone ever suggested that the administration of thyreoid tissue cures the pathological lesion upon which the disease of myxœdema rests, but these facts do not deprive either "Insulin" or thyreoid tissue of therapeutic utility. There is obviously no purpose in subjecting patients to the unpleasantness of hypodermic administration of "Insulin" or accustoming them to dependence upon it so long as dietetic measures unaided by "Insulin" suffice to establish adequate control of the disease without exceptional suffering from lack of food. It is not suggested by anybody that the dietetic treatment of diabetes should hereafter be discontinued in favour of "Insulin." There is no evidence whatever that "the remedy is too potent for safe use in very advanced conditions"; on the contrary, the greater the degree of hyperglycæmia, the safer it is to employ "Insulin" in comparatively large doses. The writer states that "material prolongation of life is improbable when the pancreatic lesion is very extensive." This is contrary to our experience and we consider it practically certain that two or three of the cases reported in our articles would not have been living at the present moment had this treatment not been employed.

The writer goes on to state that: "In the Adelaide patients 'Insulin' seems to have reduced the sugar content of the blood and consequently the glycosuria somewhat better than simple dieting. It must be remembered that very surprising results are at times obtained by scientific control of the diet, even in severe diabetes." We are perfectly able to distinguish between the effects of diet upon diabetes and the effects of "Insulin." We are aware that diabetes may frequently appear to be severe, so far as may be indicated by a heavy glycosuria, and yet prove to be perfectly controllable by diet. In almost every instance, however, this control ultimately breaks down, glycosuria and acetonæmia reappear and the diet must be successively readjusted until it falls below a level compatible with the maintenance of bearable existence or else, alternatively, the condition escapes altogether from control and terminates in fatal acetonæmia. The cases which we have reported had in several instances been under careful dietetic control for periods varying from a few months to three years and the possibilities achievable by unaided dieting were very thoroughly known. We described a case in which without "Insulin" on a diabetic dietary supplying only 684 calories per day the patient passed 84 grammes of glucose *per diem* in his urine. With two rabbit units (six new-style units) of "Insulin" *per diem* this patient passed no sugar at all on a diet containing 1,555 calories *per diem* and nearly double the carbo-hydrate formerly administered. It is certainly not fair to describe this treatment as having resulted merely in reducing the glycosuria "somewhat better than simple dieting." The effect of "Insulin," as these simple figures show, is incomparably greater than the effect of dieting alone.

Without attempting to deal further with the theoretical considerations advanced by the writer of this editorial, which, since they merely lead him to the conclusion that diabetes is an "uncanny disease," do not appear to be likely to add much of value to our comprehension of this condition, we will conclude by reverting to the practical

difficulty attending "Insulin" therapy to which he draws attention in the following words: "Whether it will ever be safe to exhibit 'Insulin' without continuous estimation of the blood sugar content cannot be determined at present. The ordinary medical practitioner is not trained as a bio-chemist and consequently he will not attempt to measure the sugar content of the blood himself."

The overcoming of this difficulty in the larger centres of population is purely a matter of organization. Doubtless the various hospitals and other institutions in the more populous communities will shortly undertake to perform blood-sugar estimations to the order of physicians whose patients reside within a convenient distance. In Adelaide these estimations are performed at a very small cost by the Adelaide Hospital and the Bio-chemical Department of the University. In the country these facilities cannot be provided, but there, on the other hand, any individual physician will only occasionally have a severe case of diabetes under his care. While the "ordinary medical practitioner" is not "trained as a bio-chemist," he is most thoroughly trained in common sense and the handling of instruments, and the suggestion that he cannot, if his isolation from large centres renders it essential, procure the necessary apparatus and perform the estimation himself is hardly complimentary to the profession. A medical student of average ability can learn to do the estimation sufficiently accurately for clinical purposes in a day. A competent nurse could readily be trained in a few days to perform the estimation to within an adequate degree of accuracy. Moreover, a "continuous estimation of blood sugar" is quite unnecessary. All that is requisite is an estimate before treatment, an estimate shortly after the initiation of treatment in order to gauge its efficacy and the adequacy of the dosage and an estimate from time to time afterwards, at such intervals as may appear advisable, to aid the physician to form an opinion of the progress of the case and, if necessary, to readjust the dosage.

Yours, etc.,

T. BRAILSFORD ROBERTSON.

C. T. CH. DE CRESPIGNY.

Adelaide,

September 5, 1923.

[In the opening sentences of the leading article published in our issue of September 1, 1923, it is clearly stated that the articles appearing in the daily press are so misleading and so dramatic that their effect must necessarily be that persons suffering from diabetes will demand injections of "Insulin," that is will determine for themselves how they are to be treated. As soon as this preparation is available in ample quantities, and this will probably be within a relatively short time, medical practitioners without facilities for laboratory work and without experience in bio-chemical technique will inevitably yield to the importunity of their patients and will inject "Insulin" without control. Macleod has pointed out that hypoglycæmia following the injection of "Insulin" is much more prolonged and much more pronounced in animals provided with small reserves of glycogen than in those with good reserves. He has stated that: "It is significant that a well-fed animal may withstand many times the dose of 'Insulin' that would prove fatal to one that was starved." He also has stated: "On account of its practical significance it should be pointed out that it is because of the poverty of the glycogen reserves that the blood sugar of diabetic patients treated with 'Insulin' is more apt to fall suddenly to a dangerously low level than in normal persons." If this preparation is given without control, on the demand of patients rather than on the advice of the practitioners, catastrophes are inevitable. It is impossible to recognize the onset of hypoglycæmic symptoms unless a control of the sugar content of the blood is being exercised. That "Insulin" has been employed in the treatment for over a year without the record of a single death attributable to it does not alter our contention. Clinicians like Dr. de Crespigny will not meet with these disasters for they are experienced in the conduct of treatment requiring bio-chemical control.

The second point also calls for a reply. From Dr. de Crespigny's article and from the articles published in the medical press elsewhere it is evident that "Insulin" is a valuable therapeutic agent when administered under proper control. The point at issue is whether sufficient information is yet available to determine the extent of its value in the treatment of diabetes. Dr. de Crespigny has published short clinical records in regard to six patients. No other reports of patients treated by injections of "Insulin" have been published in Australia. His article is a careful and clear exposition by a very competent practitioner. But it is based on only six cases. The first patient improved under the treatment, but from the table of the metabolism it will be seen that regular injections of "Insulin" together with severe restriction in diet has not reduced the blood sugar to the normal level. The second patient is also improved, but his blood sugar content is still raised. The third patient is a child. He has manifested considerable clinical improvement, which is all the more remarkable because of the infrequency of improvement when dietetic treatment alone is employed in children. The last blood sugar estimation recorded, however, was 0.22%, a high figure. The improvement in the fourth patient does not seem to be very great. "Insulin" was given to the fifth patient after he had started to improve, but Dr. de Crespigny attributes the dramatic change in his condition to the preparation and his judgement must be accepted. The sixth patient was not influenced by "Insulin." That she died of broncho-pneumonia and not of coma is immaterial, for the graph demonstrates clearly that the blood sugar content was uninfluenced by the drug. The seventh patient received three doses. The graph reveals an almost straight line of the blood sugar curve commencing before the "Insulin" was given. On these seven case records it is not possible to determine the exact value of "Insulin" in the treatment of diabetes. The writers state that no one has ever suggested that this preparation cures diabetes. This claim has been made times without number in the daily press and it has been necessary for many bio-chemists and physicians to correct this erroneous impression by the bald statement that it does not cure. The Commonwealth Serum Laboratories in some of their advertisements have emphasized this.

In the last place the signatories of the letter would entrust a student of average ability to carry out the estimations after one day's training and a competent nurse after training for a few days. That the average country practitioner of some years' standing is not trained to carry out bio-chemical tests is common knowledge. This work demands practice in laboratory technique. The inexperienced man will have difficulty in delivering a cubic centimetre of any fluid from a pipette. The busy general practitioner is quite willing to admit that this work is not within his sphere of activity and he will not attempt it. Some years ago we suggested that the general practitioner should undertake some of the simpler examinations in hæmatology, but we were met with a storm of protest from the general practitioners themselves. We admit that it would be possible to train any person of ordinary intelligence to carry out this test mechanically. But the test has to be carried out with a sense of responsibility and with a knowledge of the reason for which it is required.—EDITOR.]

REMOVAL OF TONSILS.

SIR: Does anyone ever "Sluder" a tonsil? I fail myself to see how it is possible or desirable to use "Sluder's" modification of Whillis and Pybus's method. They introduced the "reverse" operation and it is only fair to our English brethren to drop the term "Sluder" altogether.

Yours, etc.,

W. KENT HUGHES.

22, Collins Street, Melbourne.

September 14, 1923.

Congress Notes.

THE AUSTRALASIAN MEDICAL CONGRESS (BRITISH MEDICAL ASSOCIATION).

Travelling Arrangements.

CONCESSION tickets will be issued to members attending the Australasian Medical Congress (British Medical Association) in Melbourne from November 12 to 17, 1923, and their wives by the Commonwealth and State Railway Commissioners at two-thirds of the single fare both for the forward and for the return journey. Members travelling on these concession tickets will not be able to arrive in Melbourne before Thursday, November 8, 1923. Those desiring to be in Melbourne during the period of the Melbourne Cup Meeting will have to pay the full railway fares.

Enrolment.

The attention of members is drawn to the form of application for enrolment which appears on page ix. of the advertisements in this issue. The form can be cut out without defacing the reading matter of the journal. Members are requested to announce their intention of joining the Congress through the local secretaries as soon as possible. Late notification entails much unnecessary work on the part of the Executive Committee and may lead to insufficient preparations being made for the entertainment of the members of Congress. In addition the members may experience great difficulty in securing accommodation unless application for rooms be made well in advance.

Medical Matters in Parliament.

DR. STANLEY S. ARGYLE, M.L.A., has been appointed on September 6, 1923, Chief Secretary and Minister of Public Health in the Victorian Legislature. Notwithstanding the fact that Dr. Argyle has but a short parliamentary career, his ability as an exceptionally clear thinker and safe guide both in hygienic and in national matters has placed him in the front rank among members of Parliament. The Premier has done wisely in selecting Dr. Argyle as Chief Secretary and Minister of Public Health. The medical profession, not only in Victoria, but also in the other States of the Commonwealth, congratulate first of all the people of Australia on having secured so sound a controller of their most important affairs, secondly themselves, in that the profession reaps the advantage of his position and last but not least Dr. Argyle himself.

Medical Appointments.

DR. R. R. HATHERALL (B.M.A.) and DR. WILLIAM C. WOODS (B.M.A.) have been appointed Government Medical Officers at Mittagong and at Albury, respectively, in New South Wales.

* * * *

PROFESSOR H. G. CHAPMAN (B.M.A.) has been appointed Medical Referee for the State of New South Wales, excluding the County of Yancowinna, in respect of the disease of lead poisoning and its sequelæ as mentioned in Schedule Three of the *Workmen's Compensation Act, 1916*.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xviii.

AUSTIN HOSPITAL, MELBOURNE: Resident Medical Officer.
ROYAL ALEXANDRA HOSPITAL FOR CHILDREN, SYDNEY: Registrar.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney	Australian Natives' Association Ashfield and District Friendly Societies' Dispensary Balmain United Friendly Societies' Dispensary Friendly Society Lodges at Casino Leichhardt and Petersham Dispensary Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney Marrickville United Friendly Societies' Dispensary North Sydney United Friendly Societies People's Prudential Benefit Society Phœnix Mutual Provident Society
VICTORIA: Honorary Secretary, Medical Society Hall, East Melbourne	All Institutes or Medical Dispensaries Australian Prudential Association Proprietary, Limited Mutual National Provident Club National Provident Association
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane	Brisbane United Friendly Society Institute Stannary Hills Hospital
SOUTH AUSTRALIA: Honorary Secretary, 12, North Terrace, Adelaide	Contract Practice Appointments at Renmark Contract Practice Appointments in South Australia
WESTERN AUSTRALIA: Honorary Secretary, Saint George's Terrace, Perth	All Contract Practice Appointments in Western Australia
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington	Friendly Society Lodges, Wellington, New Zealand

Diary for the Month.

SEP. 25.—New South Wales Branch, B.M.A.: Medical Politics Committee; Organization and Science Committee.
SEP. 26.—Western Medical Association (Parkes), New South Wales.
SEP. 27.—South Australian Branch, B.M.A.: Branch.
SEP. 27.—Brisbane Hospital for Sick Children: Clinical Meeting.
SEP. 28.—New South Wales Branch, B.M.A.: Branch; Election of two members of Federal Committee.
SEP. 28.—Queensland Branch, B.M.A.: Council.
SEP. 30.—Victorian Branch, B.M.A.: Election of two members to Federal Committee.
OCT. 1.—Victorian Branch, B.M.A.: Election of Representatives of Divisions.
OCT. 2.—New South Wales Branch, B.M.A.: Council (Quarterly).
OCT. 3.—Victorian Branch, B.M.A.: Branch.
OCT. 5.—New South Wales Branch, B.M.A.: Annual Meeting of Delegates of Local Associations with Council.
OCT. 5.—Queensland Branch, B.M.A.: Branch.
OCT. 6.—New South Wales Branch, B.M.A.: Annual Meeting of Delegates of Local Association with Council.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, B.M.A. Building, 30-34, Elizabeth Street, Sydney. (Telephone: B. 4635.)

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and book-sellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.